September 28, 2023

Anumana, Inc.
% Alexia Haralambous
Senior Principal
RQM+
2251 San Diego Ave, Suite B-257
San Diego, California 92110

Re: K232699
Trade/Device Name: Low Ejection Fraction AI-ECG Algorithm
Regulation Number: 21 CFR 870.2380
Regulation Name: Cardiovascular Machine Learning-Based Notification Software
Regulatory Class: Class II
Product Code: QYE
Dated: September 3, 2023
Received: September 5, 2023

Dear Alexia Haralambous:

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,

Robert T. Kazmierski -S

for

LCDR Stephen Browning
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K232699

Device Name
Low Ejection Fraction AI ECG Algorithm

Indications for Use *(Describe)*
The Anumana Low Ejection Fraction AI-ECG Algorithm is software intended to aid in screening for Left Ventricular Ejection Fraction (LVEF) less than or equal to 40% in adults at risk for heart failure. This population includes, but is not limited to:

- patients with cardiomyopathies
- patients who are post-myocardial infarction
- patients with aortic stenosis
- patients with chronic atrial fibrillation
- patients receiving pharmaceutical therapies that are cardiotoxic, and
- postpartum women.

Anumana Low Ejection Fraction AI-ECG Algorithm is not intended to be a stand-alone diagnostic device for cardiac conditions, should not be used for monitoring of patients, and should not be used on ECGs with a paced rhythm.

A positive result may suggest the need for further clinical evaluation in order to establish a diagnosis of Left Ventricular Ejection Fraction (LVEF) less than or equal to 40%. Additionally, if the patient is at high risk for the cardiac condition, a negative result should not rule out further non-invasive evaluation.

The Anumana Low Ejection Fraction AI-ECG Algorithm should be applied jointly with clinician 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.

510(k) Summary
Low Ejection Fraction AI ECG Algorithm
K232699

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Date Summary Prepared: September 22, 2023
Proprietary Name of Device: Low Ejection Fraction AI ECG Algorithm
Common or Usual Name: ECG AI analysis tool
Classification Panel: Cardiology
Regulation Number: 21 CFR § 870.2380
Regulation Name: Cardiovascular machine learning-based notification software
Regulation Class: Class II
Product Code: QYE

1 Predicate Device

Device Name: VIZ HCM
Manufacturer: Viz.ai
Application Number: DEN230003

2 Device Description

The Low Ejection Fraction AI-ECG Algorithm interprets 12-lead ECG voltage times series data using an artificial intelligence-based algorithm. The device analyzes 10 seconds of a single 12-lead ECG acquisition, and within seconds provides a prediction of likelihood of LVEF (ejection fraction less than or equal to 40%) to third party software. The results are displayed by the third-party software on a device such as a smartphone, tablet, or PC. The Low Ejection Fraction AI-ECG Algorithm was trained to predict Low LVEF using positive and control cohorts, and the prediction of Low LVEF in patients is generated using defined conditions and covariates.
The Low Ejection Fraction AI-ECG Algorithm device is intended to address the unmet need for a point-of-care screen for LVEF less than or equal to 40% and is expected to be used by

cardiologists, front-line clinicians at primary care, urgent care, and emergency care settings, where cardiac imaging may not be available or may be difficult or unreliable for clinicians to operate. Clinicians will use the Low Ejection Fraction AI-ECG Algorithm to aid in screening for LVEF less than or equal to 40% and making a decision for further cardiac evaluation.

3 Intended Use/Indications for Use

The Anumana Low Ejection Fraction AI-ECG Algorithm is software intended to aid in screening for Left Ventricular Ejection Fraction (LVEF) less than or equal to 40% in adults at risk for heart failure. This population includes, but is not limited to:

- patients with cardiomyopathies
- patients who are post-myocardial infarction
- patients with aortic stenosis
- patients with chronic atrial fibrillation
- patients receiving pharmaceutical therapies that are cardiotoxic, and
- postpartum women.

Anumana Low Ejection Fraction AI-ECG Algorithm is not intended to be a stand-alone diagnostic device for cardiac conditions, should not be used for monitoring of patients, and should not be used on ECGs with a paced rhythm.

A positive result may suggest the need for further clinical evaluation in order to establish a diagnosis of Left Ventricular Ejection Fraction (LVEF) less than or equal to 40%. Additionally, if the patient is at high risk for the cardiac condition, a negative result should not rule out further non-invasive evaluation.

The Anumana Low Ejection Fraction AI-ECG Algorithm should be applied jointly with clinician judgment.

4 Technological Characteristics

The subject device, Anumana's Low Ejection Fraction AI-ECG Algorithm, is a Software as a Medical Device (SaMD) provided as a software module packaged in a Docker container. The Low Ejection Fraction AI-ECG Algorithm does not provide a graphical user interface (GUI) of its own. It is integrated with other medical systems such as Electronic Medical Record (EMR) systems or ECG Management Systems (EMS). The third-party integrating software furnishes a 12-lead ECG digital waveform as input to the Low Ejection Fraction AI-ECG Algorithm and records the algorithm output for display via the integrated medical system or for printing in an offline report.

5 Summary of Clinical Performance Data

The performance characteristics for the Low Ejection Fraction AI-ECG Algorithm have been clinically validated for the presence of a low ejection fraction of less than or equal to 40% in patients, with a sensitivity and specificity greater than the study's predetermined acceptance criteria (80%).

Table 1: Performance Characteristics

Performance Characteristic	Value
Sensitivity	80% or higher
Specificity	80% or higher

Algorithm Training

To develop the Anumana Low Ejection Fraction AI-ECG (Low EF ECG-AI) algorithm, 93,722 patients with an ECG and transthoracic echocardiogram (TTE) performed within a 2-week interval were identified from a research use authorized clinical database from Mayo Clinic. For each patient, the left ventricular ejection fraction (LVEF) measurement from the earliest TTE was selected and paired with the closest ECG recording within a 2-week interval of the TTE. The disease cohort was defined as LVEF ≤ 40% and consisted of 11% of the overall cohort. The control cohort was defined as LVEF > 40% and consisted of 89% of the overall cohort. The cohorts were split into training (50%), tuning (20%) and set-aside testing (30%) datasets. Within the set-aside test set, the sensitivity and specificity of the algorithm were 85.7% and 84.2%, respectively.

Performance analyses were also conducted in subgroups of age, sex, and race. Within the training set-aside test dataset, 91.2% of patients were White, 1.4% Black/African American, 1.3% Asian, 0.4% American Indian and 5.7% were of other or unknown races. Patients were 57.6% male and 43.4% female. The average age was 61.5 (± 16.4) years and 11.2% of patients were under age 40, 10.0% were 40-49, 18.1% were 50-59, 25.9% were 60-69, 22.3% were 70-79, and 12.5% were over 80.

Summary of Clinical Validation

Study Design

The performance profile of the Anumana Low Ejection Fraction AI-ECG (Low EF AI-ECG) algorithm was validated in a retrospective study of 16,000 patient records across 4 health systems across the United States and 16,000 patients. The objective of the study was to establish the diagnostic performance of the device for the purpose of detecting the presence of an EF ≤ 40% in a clinically and demographically diverse population. The sole inclusion criteria for a subject was age ≥ 18 and the availability of at least one digital 12-lead ECG paired with an echocardiogram with quantitative left ventricular ejection fraction (LVEF) information within 30 days following the date of the ECG. Candidate cases were identified in reverse chronological order from the date the site was activated. For each patient, the most recent echocardiogram was paired with the most recent ECG (without pacing present) acquired for that patient prior to the echocardiogram, up to the 30 days limit. Four models of 12-L ECGs (GE Dash 3000, GE MAC® 5500 Resting Analysis System, GE MAC VU360 Resting ECG, and Philips PageWriter TC70 ECG machines (model 860315) were represented in the ECG inputs to the algorithm.

Summary of Study Results

Each of the 4 sites contributed 4,000 patient-ECG pairs to a final pool of 16,000 patient-ECG pairs. The study sample was representative of the US population and was 65.9% White, 11.0%

Hispanic, 10.1% Black/African American, 5.3% American Indian or Alaska Native, 2.2% Asian, and 0.4% Native Hawaiian or Pacific Islander. The sample consisted of 52% male and 48% female participants. The average age as 66 and 11.6% of participants were under age 40, 9.2% were 40-49, 15.8% were 50-59, 22.8% were 60-69, 21.6% were 70-79, and 19% were over 80. A total of 2,040 records were excluded as a result of the quality checks performed by the Anumana Low Ejection Fraction AI-ECG (Low EF AI-ECG) algorithm.

Within this diverse study sample, a total of 1,096 LVEF ≤ 40% cases were identified (prevalence of 7.9%) from 13,960 samples. The Anumana Low EF ECG-AI device achieved a sensitivity of 84.5% (95% CI of 82.2% to 86.6%), a specificity of 83.6% (95% CI of 82.9% to 84.2%), a positive predictive value of 30.5% (PPV, 95% CI of 28.8% to 32.1%), and a negative predictive value of 98.4% (NPV, 95% CI of 98.2% to 98.7%). Results are provided in **Figure 1: Matrix of primary results** with subgroup analyses results provided in **Table 2: Subgroup Analyses.**

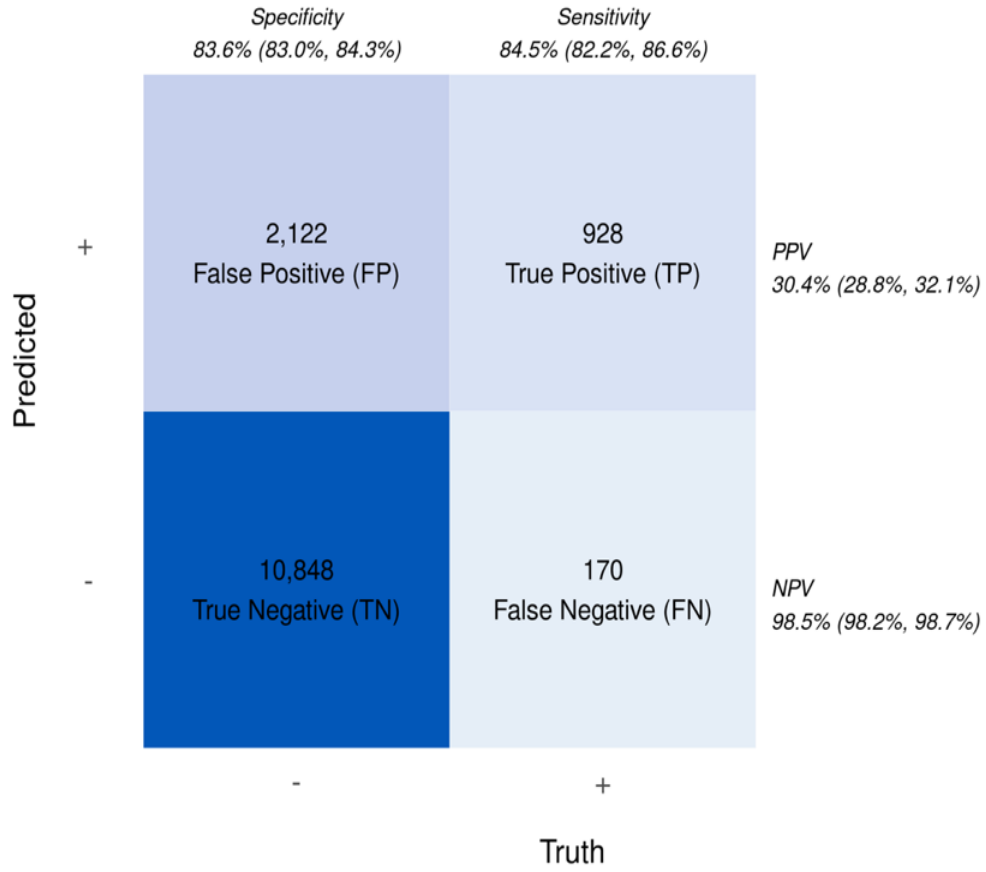

Figure 1: Matrix of primary results

Subgroup Analyses

Subgroup assessments of diagnostic performance were conducted to determine if there was heterogeneity in device performance across clinical sites, demographics, clinical characteristics, conduction disorders, ECG manufacturer, and ECG devices. To assess for heterogeneity, Breslow-Day tests for the strata were conducted on the odds ratio for condition presence given a positive ECG-AI result. The results are summarized in **Table 2** below.

Table 2: Subgroup Analyses

Subgroup Analysis	Result of Test for Heterogeneity
Clinical Site	Not statistically significant
Biological Sex	Not statistically significant
Race/Ethnicity	Not statistically significant
Age Group	Diagnostic performance varied across age strata ($p < 0.01$). The diagnostic odds ratio was higher than the overall estimate in patients aged 40 to 69 years and lower in younger and older patients. In younger patients, sensitivity was lower while specificity was higher, whereas in patients of advanced age, sensitivity was higher while specificity was lower.
Clinical Characteristics	• Diagnostic performance varied across body mass index strata ($p = 0.02$), with the lowest diagnostic performance observed in underweight (BMI <18.5 kg/m2) participants and the highest diagnostic performance observed in overweight (BMI 25+ to <30) and obese (BMI 30+) participants. • Diagnostic performance varied across certain elements of medical history derived from ICD9/ICD10 codes in patient medical records. The diagnostic odds ratio was lower in patients with prior history of heart failure ($p<0.01$), myocardial infarction ($p<0.01$) and coronary revascularization ($p=0.07$). In each of these cases, the disease prevalence was high (>17% for the three conditions) and the algorithm had higher sensitivity and lower specificity. This combination, at the higher prevalence values, resulted in robust positive predictive value (>35%) and negative predictive value (>94%).
Conduction Disorders	Not statistically significant
ECG Manufacturer	Not statistically significant
ECG Device	Not statistically significant

6 Summary of Non-Clinical Performance Data

The performance characteristics for the Low Ejection Fraction AI-ECG Algorithm have been evaluated with the following non-clinical testing: software verification and validation (per IEC 62304), cybersecurity, labeling validation, and human factors.

Substantial Equivalence Conclusion

The subject device, Anumana Low Ejection Fraction AI-ECG Algorithm, is substantially equivalent to the predicate device Viz HCM (DEN230003). The devices have similar intended uses, principles of operation, and technical characteristics. Where differences occur between the subject device and the predicate, results of clinical performance and results of non-clinical verification and validation demonstrate that the subject device is as safe and as effective as the predicate.

Table 3: Substantial Equivalence Comparison of Subject Device to the Predicate

	Subject Device	Predicate Device	
Product Name	**Anumana Low Ejection Fraction AI-ECG Algorithm**	**Viz HCM**	**Comparison**
Application No.	K232699	DEN230003	-
Product Codes	QXX DQK	QXO	-
Regulation No.	21 CFR 870.2380	21 CFR 870.2380 21 CFR 870.1425	-
Regulation Name	Cardiovascular machine learning-based notification software	Cardiovascular machine learning-based notification software	-
Rx / OTC	Rx	Rx	Same
Intended Use/ Indications for Use	The Anumana Low Ejection Fraction AI-ECG Algorithm is software intended to aid in screening for Left Ventricular Ejection Fraction (LVEF) less than or equal to 40% in adults at risk for heart failure. This population includes, but is not limited to: • patients with cardiomyopathies • patients who are post-myocardial infarction • patients with aortic stenosis • patients with chronic atrial fibrillation • patients receiving pharmaceutical therapies that are cardiotoxic, and • postpartum women. Anumana Low Ejection Fraction AI-ECG Algorithm is not intended to be a stand-alone diagnostic device for	Viz HCM, a standalone electrocardiogram (ECG) analysis software to identify patients 18 or older for further follow-up for hypertrophic cardiomyopathy (HCM), a rare condition in which the heart muscle becomes abnormally thick and makes it difficult for the heart to pump blood. This device can analyze recordings from compatible 12-lead ECGs, detect signs associated with HCM, and allow the user to view the ECG and software analysis. The device does not provide a diagnosis of HCM and is not intended for use on patients with implanted pacemakers	Similar – The subject device is intended to aid in screening for Left Ventricular Ejection Fraction (LVEF) less than or equal to 40% in adults at risk for heart failure, whereas the predicate device is an analysis software used to identify patients for further follow-up for hypertrophic cardiomyopathy (HCM).

	Subject Device	Predicate Device	
Product Name	**Anumana Low Ejection Fraction AI-ECG Algorithm**	**Viz HCM**	**Comparison**
	cardiac conditions, should not be used for monitoring of patients, and should not be used on ECGs with a paced rhythm. A positive result may suggest the need for further clinical evaluation in order to establish a diagnosis of Left Ventricular Ejection Fraction (LVEF) less than or equal to 40%. Additionally, if the patient is at high risk for the cardiac condition, a negative result should not rule out further non-invasive evaluation. The Anumana Low Ejection Fraction AI-ECG Algorithm should be applied jointly with clinician judgment.		
Operational Mode	Spot check	Spot check	Same
Motion	None	Hemosphere Advanced Monitoring Platform and ClearSight Module (K201446) WorkMate Claris System (K210392)	Similar – The subject device is a SaMD that does not need to take into account motion correction.
Patient Population	Adults	Adults	Same
Environment of Use	Primary care, urgent care, and emergency care settings	Hospital and Pre-Hospital Setting	Similar – Both devices are to be used in professional healthcare settings

	Subject Device	Predicate Device	
Product Name	**Anumana Low Ejection Fraction AI-ECG Algorithm**	**Viz HCM**	**Comparison**
Algorithm	Machine learning based algorithm with a predetermined change control plan (PCCP)	Machine learning based algorithm	Similar – The subject device submission proactively pre-specifies intended modifications (and their method of implementation) that do not require additional marketing submission.
Algorithm Calculation and Output	Detection of LVEF (Left Ventricular Ejection Fraction less than or equal to 40%) from an ECG signal	Presence of signs associated with HCM derived from an ECG signal	Similar – Both devices identify a single cardiovascular condition
Ground Truth for Model Training	Transthoracic echocardiogram (TTE) with disease	Cardiologist adjudicated signs associated with a disease using an ECG waveform	Similar – Both devices rely upon established clinical diagnostic methods as ground truth
Physiological Parameter Inputs	12-Lead ECG waveform in digital format	Parameters gathered from the Hemosphere Advanced Monitoring Platform and ClearSight Module (K201446) and WorkMate Claris System (K210392). Includes oximetry, heart rate, and additional cardiac parameters (e.g., blood pressure) using an EKG.	Similar – Both devices utilize ECG digital waveforms as input
Data Displayed	Algorithm output is provided to third party software that displays the result to clinicians. Output provided for each ECG is “Low LVEF Detected” “Low LVEF Not Detected” or “Error”).	Device flags suspected ECGs and categorizes patients as requiring further follow up.	Similar – Both devices provide data suggesting the likelihood of a cardiovascular disease or condition for further referral or diagnostic follow-up.
Hardware	Compatible 12-Lead diagnostic ECG machines with 500Hz digital output	Hemosphere Advanced Monitoring Platform and ClearSight Module (K201446) and WorkMate Claris System (K210392)	Similar – Both devices are compatible with devices providing digital ECG outputs

	Subject Device	Predicate Device	
Product Name	**Anumana Low Ejection Fraction AI-ECG Algorithm**	**Viz HCM**	**Comparison**
Software	Anumana proprietary algorithm and application	Viz.AI proprietary algorithm and application	Similar – Both devices incorporate their own proprietary algorithms and applications.