

**DE NOVO CLASSIFICATION REQUEST FOR
Viz HCM**

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Cardiovascular machine learning-based notification software. Cardiovascular machine learning-based notification software employs machine learning techniques to suggest the likelihood of a cardiovascular disease or condition for further referral or diagnostic follow-up. The software identifies a single condition based on one or more non-invasive physiological inputs as part of routine medical care. It is intended as the basis for further testing and is not intended to provide diagnostic quality output. It is not intended to identify or detect arrhythmias.

NEW REGULATION NUMBER: 21 CFR 870.2380

CLASSIFICATION: Class II

PRODUCT CODE: QXO

BACKGROUND

DEVICE NAME: Viz HCM

SUBMISSION NUMBER: DEN230003

DATE DE NOVO RECEIVED: January 10, 2023

SPONSOR INFORMATION:

Viz.ai, Inc.
201 Mission St., 12th Floor
San Francisco, California 94105

INDICATIONS FOR USE

The Viz HCM is indicated as follows:

Viz HCM is intended to be used in parallel to the standard of care to analyze recordings of 12-lead ECG made on compatible ECG devices. Viz HCM is capable of analyzing the ECG, detecting signs associated with hypertrophic cardiomyopathy (HCM), and allowing the user to view the ECG and analysis results. Viz HCM is indicated for use on 12-lead ECG recordings collected from patients 18 years of age or older. Viz HCM is not intended for use on patients with implanted pacemakers. Viz HCM is limited to analysis of ECG data and should not be used in-lieu of full patient evaluation or relied upon to

make or confirm diagnosis. Viz HCM identifies patients for further HCM follow-up and does not replace the current standard of care methods for diagnosis of HCM. The results of the device are not intended to rule-out HCM follow-up.

LIMITATIONS

The sale, distribution, and use of the Viz HCM are restricted to prescription use in accordance with 21 CFR 801.109.

The device identifies patients for further HCM follow-up and does not replace the current standard of care methods for diagnosis of HCM. The results of the device are not intended to rule-out HCM follow-up.

The device is not intended for use on patients with implanted pacemakers.

The results of the device should not be used in lieu of full patient evaluation.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The Viz HCM ECG Analysis Algorithm (HCM Algorithm) is a machine learning-based software algorithm that analyzes 12-lead electrocardiograms (ECGs) for characteristics suggestive of hypertrophic cardiomyopathy (HCM). The mobile software module enables the end user to receive and toggle notifications for ECGs determined by the Viz HCM ECG Analysis Algorithm to contain signs suggestive of HCM.

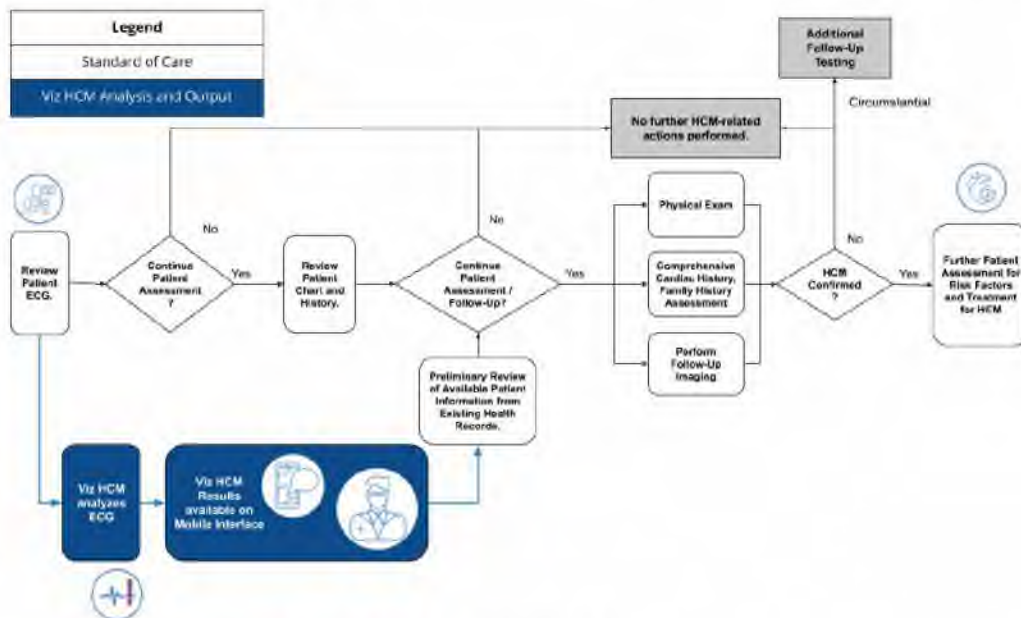


Figure 1. Clinical Workflow Diagram

The Viz HCM is a Software as a Medical Device (SaMD) intended to analyze ECG signals collected as part of a routine clinical assessment, independently and in parallel to the standard of care. Viz HCM is a combination of software modules that consists of an ECG analysis software algorithm and mobile application software module.

SUMMARY OF NONCLINICAL/BENCH STUDIES

Nonclinical studies conducted for the Viz HCM system are summarized below.

SOFTWARE

The software was reviewed according to the "[Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices](#)" dated May 11, 2005.

Appropriate software documentation consistent with a "Moderate" level of software concern were provided.

The software documentation included a detailed description of the machine learning model, the model inputs and outputs, and the supported patient population. Integration testing was conducted in the intended software system. Testing accounted for the impact of and variability between different ECG acquisition hardware. The ECG hardware controls included a description of input ECG signal control measures and mitigations for user error and system components on output accuracy.

Cybersecurity was reviewed in accordance with the FDA guidance document "[Content of Premarket Submissions for Management of Cybersecurity in Medical Devices](#)" dated October 2, 2014.

PERFORMANCE TESTING – MODEL DEVELOPMENT AND INTERNAL VALIDATION

The data for algorithm development was collected from different US and Non-US (OUS) sources. The data contains both HCM Positive (obstructive and nonobstructive) and HCM Negative examples including random ECG samples (random control) and enrichment for conditions differential for and associated with HCM (negative controls). The data is diverse with respect to the age, sex, and health status of the patient, as well as the data source from which the ECG data was taken. Efforts were made to sample the data from data sources from ethnically diverse regions so as to promote ethnic diversity in the training and internal validation datasets.

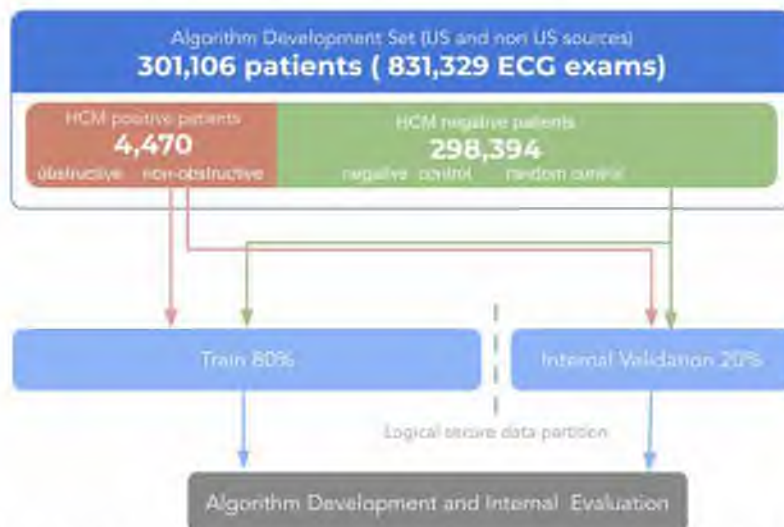


Figure 2. Distribution and separation of training and internal validation data

Refer to Table 9 in the labeling section of this document for full demographics of training and internal validation datasets.

The development dataset was split into disjoint and secured training and internal validation partitions. The partitions were created using a hash function on a patient-anonymized unique identifier (patient UID) to ensure consistency across all development phases and across different models and datasets and prevents different studies of the same patient being allocated to more than one partition.

PERFORMANCE TESTING – USABILITY

The usability of the Viz HCM system was assessed per EN 62366-1 “Medical Devices-Part 1: Application of usability engineering to medical devices” dated 2015 + A1:2020 and the FDA guidance document “[Applying Human Factors and Usability Engineering to Medical Devices](#)”. A use-related risk analysis (URRA) and system risk analysis (RA) were performed to identify use-related hazards and critical tasks. The study recruited 16 representative clinical users who were assessed within two (2) use scenarios for task completion according to correct use, user error, close calls, or use difficulty.

- There were no use errors during the study
- All participants demonstrated full understanding of the intended use, device output (i.e., the HCM flag), and that they would not rely on the device to make a diagnosis
- 15/16 (93%) participants acknowledged the HCM flag during the session to review the ECG record

This testing demonstrated that the intended users of the product can perform the product’s intended use in the expected use environment. It also demonstrated that the intended users could adequately comprehend the labeling.

SUMMARY OF CLINICAL INFORMATION

OVERVIEW

Model testing was performed on a dataset which was acquired from a retrospective study to assess the performance of Viz HCM in the identification of suspected HCM findings in ECG as compared to the clinical finding of HCM as established by cardiologist chart and imaging review of historical patient data. The objectives of the study were to assess the performance of the device in terms of sensitivity, specificity, and device positive predictive value (PPV), and conduct additional analyses to assess the device performance for detection of suspected HCM in different sub-populations. This was a non-significant risk study using historical patient data and did not involve enrollment of any human beings. Due to the retrospective nature of the study, no adverse events were expected or observed. The Institutional Review Board (IRB) overseeing the study at participating hospitals waived the need for patient informed consent.

A total of 3,196 (291 HCM-Positive and 2905 HCM-Negative) ECG cases were included in the performance assessment for the pivotal study. Patient cases were selected from 3 hospitals representing a combination of academic and community hospitals between July 1, 2017, and June 30, 2022. Two (2) of the three (3) sites providing data were from the Boston, Massachusetts area which are racially and ethnically diverse in terms of the local African American, Asian, and Multi-Race (two or more) populations. The third site was in Salem, Massachusetts which was predominantly Caucasian or Latino. All three sites provided data from geographic areas with similar proportions of Hispanic or Latino individuals in the local population, which were also similar to the proportion of the Hispanic or Latino population in the USA overall. The proportions of obstructive and non-obstructive HCM were roughly equal. See Table 2 for full demographic information.

TRUTHING PROCESS

For each HCM-Positive or HCM-Negative case, a single cardiologist performed a chart and imaging review (where available) for the patient to confirm the presence of HCM according to predefined guidelines using either the Cornell criteria or the Sokolow-Lyon criteria. In addition, ECGs were annotated for the presence of different features and pathologies. ECGs determined to contain a pacemaker or corrupt lead were excluded during ECG annotations.

For HCM-Positive cases, the cardiologist assessed the patient chart and imaging to confirm the presence of HCM and if confirmed, the degree of obstruction (either non-obstructive or obstructive). HCM-Negative cases were reviewed for the presence or mention of HCM in the patient chart, along with any available imaging to rule out HCM. If the patient chart and imaging confirmed the presence of HCM, the patient was moved from the HCM-Negative cohort to the HCM-Positive cohort. As part of a secondary assessment, a selection of 60 cases (30 HCM-Positive cases and 30 HCM-Negative) were truthed by a second cardiologist to perform an analysis of agreement/consistency in confirmation of HCM.

In the study, the ICD-10 Code was used to sample HCM-Positive and HCM-Negative patients prior to truthing. During the truthing process, HCM-Negative patient cases were confirmed if there were no notes related to HCM in the patient chart. These would be determined as HCM-Negative by the lack of ICD-9/10 code for HCM as was the case with algorithm development. For HCM-Negative patient cases with available imaging or HCM-Positive cases, the additional chart review and review of imaging provided more confidence into the label with imaging

evidence as established by the initial sampling of the ICD-9/10 codes associated with the patient diagnosis (or lack of HCM diagnosis).

The study results are in Table 1 below.

Performance Measure	Results
Sensitivity	68.4% (95% CI: 62.8% - 73.5%)
Specificity	99.1% (95% CI: 98.7% - 99.4%)
PPV (prevalence of 0.002)	13.7% (95% CI: 10.1% - 19.9%)

Table 1. Clinical Testing Results

Refer to Table 9 for full demographics of training and internal validation datasets.

In addition, subgroup analyses were conducted by:

- Hospital site
- ECG device make/model
- Gender
- Age
- Race
- Ethnicity
- HCM Characterization (i.e., obstructive vs. non-obstructive)

Subgroup	AUC (95% CI)	True positive	False negative	Sensitivity (95% CI)	True negative	False positive	Specificity (95% CI)
BWH	0.982 (0.971,0.990)	82	29	73.9 (65.0,81.2)	957	11	98.9 (98.0,99.4)
MGH	0.986 (0.980,0.992)	75	32	70.1 (60.8,78.0)	974	4	99.6 (98.9,99.9)
SH	0.948 (0.915,0.970)	42	31	57.5 (46.1,68.2)	949	10	99.0 (98.1,99.5)

Table 2: Subgroup Analysis by Site

Subgroup	True positive	False negative	Sensitivity (95% CI)
Obstructive	97	45	68.3 (60.2,75.4)
Non-obstructive	102	47	68.5 (60.6,75.4)

Table 3: Subgroup Analysis by HCM type

Subgroup	AUC (95% CI)	True positive	False negative	Sensitivity (95% CI)	True negative	False positive	Specificity (95% CI)
Female	0.979 (0.971,0.985)	85	54	61.2 (52.8,68.9)	1494	7	99.5 (99.0,99.8)
Male	0.971 (0.954,0.984)	114	38	75.0 (67.5,81.2)	1386	18	98.7 (98.0,99.2)

Table 4: Subgroup Analysis by gender

Subgroup	AUC (95% CI)	True positive	False negative	Sensitivity (95% CI)	True negative	False positive	Specificity (95% CI)
< 40 years	0.977 (0.932,1.000)	32	6	84.2 (69.2,92.9)	485	1	99.8 (98.7,100.1)
40 – 65 years	0.973 (0.963,0.982)	84	47	64.1 (55.6,71.8)	1166	12	99.0 (98.2,99.4)
> 65 years	0.973 (0.959,0.983)	83	39	68.0 (59.3,75.7)	1229	12	99.0 (98.3,99.5)

Table 5: Subgroup Analysis by age

Subgroup	AUC (95% CI)	True positive	False negative	Sensitivity (95% CI)	True negative	False positive	Specificity (95% CI)
American Indian or Alaska Native	-	0	0	-	2	0	100.0 (29.0,105.2)
Asian	0.987 (0.962,0.999)	11	4	73.3 (47.6,89.5)	93	1	98.9 (93.6,100.4)
Black	0.981 (0.961,0.994)	20	11	64.5 (46.9,79.0)	262	2	99.2 (97.1,100.0)
Native Hawaiian or Other Pacific Islander	-	0	0	-	1	0	100.0 (16.7,103.9)
White	0.972 (0.959,0.981)	149	74	66.8 (60.4,72.7)	2222	21	99.1 (98.6,99.4)
Other	1.000 (0.997,1.000)	9	0	100.0 (65.5,104.5)	192	1	99.5 (96.8,100.2)
Two or More	1.000 (1.000,1.000)	3	1	75.0 (28.9,96.6)	21	0	100.0 (81.8,102.8)
Declined	1.000 (0.956,1.000)	3	1	75.0 (28.9,96.6)	34	0	100.0 (87.9,101.9)
Unknown	0.996 (0.966,1.000)	4	1	80.0 (36.0,98.0)	53	0	100.0 (91.9,101.3)

Table 6: Subgroup Analysis by race

Subgroup	AUC (95% CI)	True positive	False negative	Sensitivity (95% CI)	True negative	False positive	Specificity (95% CI)
Hispanic	1.000 (0.995,1.000)	7	0	100.0 (59.6,105.0)	167	3	98.2 (94.7,99.6)
Non Hispanic	0.973 (0.962,0.982)	166	80	67.5 (61.4,73.0)	2485	21	99.2 (98.7,99.5)
Declined	0.989 (0.964,1.000)	11	6	64.7 (41.2,82.8)	120	0	100.0 (96.3,100.6)
Unknown	0.964 (0.923,0.990)	15	6	71.4 (49.8,86.4)	108	1	99.1 (94.5,100.3)

Table 7: Subgroup Analysis by ethnicity

Subgroup	True positive	False negative	Sensitivity (95% CI)
Obstructive	97	45	68.3 (60.2,75.4)
Non-obstructive	102	47	68.5 (60.6,75.4)

Table 8: Subgroup Analysis by HCM type

Further stratification was conducted for:

- Concurrent ECG findings and anomalies, and
- Comorbid conditions

Pediatric Extrapolation

For medical devices, the FD&C Act defines patients before their 22nd birthday as pediatric patients. In this De Novo request, data from patients between 18-21 were used to support the use of the device in patients over the age of 18.

LABELING

The labeling supports the decision, including information on all required and/or compatible parts, to grant the De Novo request for this device. The labeling includes a detailed description of the device, description of the patient population for which the device is indicated for use, a description of the intended user population, and instructions for use.

The labeling reflects the following critical intended use and limitations of the Viz HCM device:

- The device identifies patients for further HCM follow-up and does not replace the current standard of care methods for diagnosis of HCM. The results of the device are not intended to rule-out HCM follow-up.
- The device is not intended for use on patients with implanted pacemakers.
- The results of the device should not be used in lieu of full patient evaluation.

The following baseline demographic information is included in the labeling for age, race, ethnicity, sex, and HCM type.

Training (N=301,106)			Testing (N=3196)		
Sex			Sex		
Female	166,885	55.4%	Female	1640	51.3%
Male	134,221	44.6%	Male	1556	48.7%
Age			Age		
< 40	73,099	24.3%	< 40	524	16.4%
40 - 65	127,551	42.4%	40 - 65	1309	41.0%
> 65	100,456	33.4%	> 65	1363	42.6%
Race			Race		
American Indian / Alaska Native	*Data collected from multiple regions (USA and OUS) representing different races: - United States - Israel - Germany - Brazil		American Indian / Alaska Native	2	0.1%
Asian			Asian	109	3.4%
Black			Black	295	9.2%
Native Hawaiian / Pacific Islander			Native Hawaiian / Pacific Islander	1	< 0.1%
White			White	2466	77.2%
Other			Other	202	6.3%
Two or More			Two or More	25	0.8%
Declined			Declined	38	1.2%
Unknown			Unknown	58	1.8%
Ethnicity			Ethnicity		
Hispanic	*See notes for racial distribution.		Hispanic	177	5.5%
Non-Hispanic			Non-Hispanic	2752	86.1%
Declined			Declined	137	4.3%
Unknown			Unknown	130	4.1%
HCM Presence			HCM Presence		
Obstructive	3,682	1.2%	Obstructive	142	4.4%
Non-Obstructive	892	0.3%	Non-Obstructive	149	4.7%
No HCM (Negative)	296,530	98.5%	No HCM (Negative)	2905	90.9%

Table 9. Training and Test set demographics

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of cardiovascular machine learning-based notification software.

Table 10 – Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
False positive or false negative leading to incorrect treatment or diagnosis	Clinical performance testing Non-clinical performance testing Labeling
Incorrect treatment or diagnosis due to model bias or failure to adequately generalize to the intended use population	Clinical performance testing Labeling
Device used in unsupported patient population or with unsupported input/hardware	Labeling Human factors assessment Software verification, validation, and hazard analysis

Overreliance on device output for follow-up	Human factors assessment Labeling
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SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, cardiovascular machine learning-based notification software is subject to the following special controls:

- (1) Clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following must be met:
 - (i) Clinical validation must use a test dataset of real-world data acquired from a representative patient population. Data must be representative of the range of data sources and data quality likely to be encountered in the intended use population and relevant use conditions in the intended use environment. The test dataset must be independent from data used in training/development and contain sufficient numbers of cases from important cohorts (e.g., demographic populations, subsets defined by clinically relevant confounders, comorbidities, and subsets defined by hardware and acquisition characteristics) such that the performance estimates and confidence intervals of the device for these individual subsets can be characterized for the intended use population and acquisition systems (e.g., acquisition hardware or preprocessing software). Study protocols must include a description of the adjudication process(es) for determining ground truth of training and test datasets;
 - (ii) Data must be provided within the clinical validation study or using equivalent datasets to demonstrate the consistency of the output over the full range of inputs;
 - (iii) Performance goals used to determine success of clinical validation must be justified in the context of risks associated with follow-up testing;
 - (iv) Objective performance measures (e.g., sensitivity, specificity, positive predictive value or negative predictive value) must be reported with relevant descriptive or developmental performance measures. Summary level demographic information and sub-group analyses must be provided for each study site, relevant demographic sub-groups, and acquisition systems; and
 - (v) The test dataset must include a minimum of 3 geographically diverse sites, separate from sites used in training of the model.

- (2) Software verification, validation, and hazard analysis must be performed. Software documentation must include:
 - (i) A description of the model/algorithm, algorithm inputs/outputs, and supported patient population;
 - (ii) Integration testing in the intended software system or software environment; and
 - (iii) A description of the expected impact of all applicable sensor acquisition hardware characteristics on performance and any associated hardware specifications, including:
 - (A) A description of input signal / data quality control measures; and

- (B) A description of all mitigations for user error or failure of any subsystem components (including signal detection, signal analysis, data display, and storage) on output accuracy.
- (3) Human factors assessment of the intended users in the intended use environment must evaluate the risk of misinterpretation of device output.
- (4) Labeling must include:
 - (i) A summary of the performance testing methods, tested hardware, tested/supported patient population, results of the performance testing for tested performance measures/metrics, summary-level descriptions of patient demographics and associated subgroup analyses for training and test datasets, and the expected minimum performance of the device;
 - (ii) Device limitations or subpopulations for which the device may not perform as expected;
 - (iii) Warning that the user should not rely on the lack of a suspected finding to rule-out follow-up;
 - (iv) A statement that the device output should not replace a full clinical evaluation of the patient and that the output may not be sufficient as the sole basis for further testing;
 - (v) Warnings identifying sensor acquisition factors that may impact measurement results;
 - (vi) Guidance for interpretation of the measurements and typical follow-up testing; and
 - (vii) The type(s) of hardware sensor data used, including specification of compatible sensors for data acquisition.

BENEFIT-RISK DETERMINATION

The risks of the device are based on nonclinical testing as well as data collected in a clinical study described above.

Primary risk is false negatives where a subject with HCM would be said to not likely have the disease. The original clinical testing and additional analyses provided adequate information to assess the likely performance of the device in the intended use population. The specificity is sufficiently high to address the risk of false negatives and there is low risk associated with routine follow-up testing with false positives. Due to the low prevalence of the disease, the positive predictive value is low but HCM is hard to diagnose, so the risk of false positives is acceptable given the benefit of identifying HCM in otherwise asymptomatic patients. Usability testing was performed to ensure that the output is not misinterpreted as a definitive diagnosis. This testing was performed in cardiologists rather than non-specialty clinicians; however, this is likely adequate as non-cardiologists would likely be more prone to referring to further follow-up, which is the intended use of the device.

The probable benefits of the device are also based on nonclinical laboratory studies as well as data collected in a clinical study as described above.

The ability to provide additional detection of and insight into a disease that is relatively uncommon and difficult to diagnose in subjects represents a benefit to the intended patient population.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

Viz HCM is intended to be used in parallel to the standard of care to analyze recordings of 12-lead ECG made on compatible ECG devices. Viz HCM is capable of analyzing the ECG, detecting signs associated with hypertrophic cardiomyopathy (HCM), and allowing the user to view the ECG and analysis results. Viz HCM is indicated for use on 12-lead ECG recordings collected from patients 18 years of age or older. Viz HCM is not intended for use on patients with implanted pacemakers. Viz HCM is limited to analysis of ECG data and should not be used in-lieu of full patient evaluation or relied upon to make or confirm diagnosis. Viz HCM identifies patients for further HCM follow-up and does not replace the current standard of care methods for diagnosis of HCM. The results of the device are not intended to rule-out HCM follow-up. The probable benefits outweigh the probable risks for the Viz HCM. The device provides benefits, and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo for the Viz HCM is granted and the device is classified as follows:

Product Code: QXO

Device Type: Cardiovascular machine learning-based notification software

Regulation Number: 21 CFR 870.2380

Class: II