U.S. FOOD & DRUG ADMINISTRATION

March 28, 2024

Eko Health, Inc.
Sam Huang
Director of Regulatory Affairs
2100 Powell Street
Suite 300
Emeryville, California 94608

Re: K233409
Trade/Device Name: Eko Low Ejection Fraction Tool (ELEFT)
Regulation Number: 21 CFR 870.2380
Regulation Name: Cardiovascular Machine Learning-Based Notification Software
Regulatory Class: Class II
Product Code: QYE
Dated: March 27, 2024
Received: March 27, 2024

Dear Sam Huang:

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.

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.

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,

Stephen C. Browning -S

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: 06/30/2023
See PRA Statement below.

Submission Number *(if known)*

K233409

Device Name

Eko Low Ejection Fraction Tool (ELEFT)

Indications for Use *(Describe)*

Eko Low Ejection Fraction Tool (ELEFT) is a software intended to aid clinicians in identifying individuals with Left Ventricular Ejection Fraction (LVEF) less than or equal to 40%. ELEFT takes as input ECG and heart sounds and is intended for use on patients at risk for heart failure This population includes, but is not limited to, patients with: coronary artery disease; diabetes mellitus; cardiomyopathy; hypertension; and obesity.

The interpretations of heart sounds and ECG offered by the software are meant only to assist healthcare providers in assessing Left Ventricular Ejection Fraction ≤ 40%, who may use the result in conjunction with their own evaluation and clinical judgment. It is not a diagnosis or for monitoring of patients diagnosed with heart failure. This software is for use on adults (18 years and older).

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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GENERAL INFORMATION

Applicant:
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Phone: 844-356-3384

Contact Person:
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Director of Regulatory Affairs
Eko Health, Inc.

Date Prepared: March 25th, 2024

DEVICE INFORMATION

Trade/Proprietary Name: Eko Low Ejection Fraction Tool (ELEFT)
Regulation number: 21 CFR 870.2380
Regulation Name: Cardiovascular machine learning-based notification software
Regulatory Class: Class II
Product Code: QYE

PREDICATE DEVICES

- Low Ejection Fraction AI ECG Algorithm (K232699)

DEVICE DESCRIPTION

Eko Low Ejection Fraction Tool (ELEFT) is an algorithm that is intended to aid clinicians to identify individuals with Left Ventricular Ejection Fraction (LVEF) less than or equal to 40%. ELEFT takes as input ECG and heart sounds from patients at risk for heart failure. The software uses signal processing as well as machine learning algorithms, to analyze the electrocardiogram (ECG) and heart sound/phonocardiogram (PCG) recording signals generated by FDA-cleared Eko Stethoscopes and saved as .WAV file recordings in the Eko Cloud. ELEFT is a machine learning based notification software which employs machine learning techniques to suggest the likelihood of LVEF ≤ 40% for further referral or diagnostic follow-up. It is intended as the basis for further testing and is not intended to provide diagnostic quality output. As an integral part of a physical assessment, clinician's interpretations of this data can help identify previously undiagnosed left ventricular dysfunction in a patient.

The ELEFT consists of the following algorithm components:

- **Eko Low Ejection Fraction Tool API**

  The web-based API controller that handles ECG (.wav format) and sound file (.wav format) inputs and algorithm result (JSON format) outputs.

  Routes data to the appropriate deep neural network models for classification.

- **Waveform Analysis**:

  A previously FDA-cleared algorithm (K192004) is used to classify the signal quality of the ECG and heart sound. If ECG signal quality is poor, the API response is "Poor ECG Signal". Otherwise, deep convolutional neural network models are used to classify ECG and heart sound as "Normal Ejection Fraction" or "Low Ejection Fraction".

This device is solely intended to analyze signals collected by the "Eko DUO" device cleared as K170874. In the case of a positive result, consider referral for cardiology consult or echocardiogram, which can confirm the presence or absence of Low Ejection Fraction. ELEFT should not be used in lieu of an echocardiogram or other diagnostic tests. ELEFT should not be used to monitor disease progression. A negative result does not exclude Low Ejection Fraction. The device is solely intended to analyze recordings collected by healthcare professionals or other operators with at least 5 years experience in collecting clinical data.

INDICATIONS FOR USE

Eko Low Ejection Fraction Tool (ELEFT) is a software intended to aid clinicians in identifying individuals with Left Ventricular Ejection Fraction (LVEF) less than or equal to 40%. ELEFT takes as input ECG and heart sounds and is intended for use on patients at risk for heart failure. This population includes, but is not limited to, patients with: coronary artery disease; diabetes mellitus; cardiomyopathy; hypertension; and obesity.

The interpretations of heart sounds and ECG offered by the software are meant only to assist healthcare providers in assessing Left Ventricular Ejection Fraction ≤ 40% , who may use the result in conjunction with their own evaluation and clinical judgment. It is not a diagnosis or for monitoring of patients diagnosed with heart failure. This software is for use on adults (18 years and older).

SUBSTANTIAL EQUIVALENCE

Table 1: Substantial Equivalence Comparison Table

Feature	Subject Device: Eko Low Ejection Fraction Tool (ELEFT)	Predicate: Low Ejection Fraction AI ECG Algorithm (K232699)	Comparison
Regulation Number and Name	21 CFR 870.2380 Cardiovascular machine learning-based notification software	21 CFR 870.2380 Cardiovascular machine learning-based notification software	Same
Classification Product Code	QYE	QYE	Same
Indications for Use	Eko Low Ejection Fraction Tool (ELEFT) is a software intended to aid clinicians in identifying individuals with Left Ventricular Ejection Fraction (LVEF) less than or equal to 40%. ELEFT takes as input ECG and heart sounds and is intended for use on patients at risk for heart failure. This population includes, but is not limited to, patients with: coronary artery disease; diabetes mellitus; cardiomyopathy; hypertension; and obesity. The interpretations of heart sounds and ECG offered by the software are meant only to assist healthcare providers in assessing Left Ventricular Ejection Fraction ≤ 40% who may use the result in conjunction with their own evaluation and clinical judgment. It is not a diagnosis or for monitoring of patients diagnosed with heart failure. This software is for use on adults (18 years and older).	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.	Same intended use; Similar indications for cardiovascular conditions

Prescription/ OTC	Prescription Only	Prescription Only	Same
Patient Population	Patients 18 years of age and older	Patients 18 years of age and older	Same
Intended as the basis for further testing?	Yes	Yes	Same
Intended to provide diagnostic quality output?	No	No	Same
Intended to identify or detect arrhythmias?	No	No	Same
Technological Characteristics			
Mechanism of Operations	The Eko Low Ejection Fraction Tool (ELEFT) to identify individuals with Left Ventricular Ejection Fraction (LVEF) less than or equal to 40% by analyzing ECG and heart sounds from patients at risk for heart failure.	Anumana Low Ejection Fraction AI-ECG Algorithm is capable of analyzing the ECG, detecting signs associated with hypertrophic cardiomyopathy (HCM), and allowing the user to view the ECG and analysis results.	Similar. ELEFT can also analyze PCG signals when available.
Physiological Input Signals	ECG recording signals from single lead PCG recording signals (when available)	12-lead ECG waveform in digital format	Similar. ELEFT can also analyze PCG signals when available.
Software Display	Application Programming Interface (API) only, no user interface	Has user interface	Different. The technology characteristic difference does not raise different questions of safety and effectiveness

PERFORMANCE DATA - NONCLINICAL TESTING SUMMARY

The performance characteristics for the Eko Low Ejection Fraction Tool (ELEFT) have been evaluated with the following non-clinical testing: software unit, integration and system level verification testing consistent with the IEC 62304 standard, and cybersecurity testing.

PERFORMANCE DATA - CLINICAL PERFORMANCE

ELEFT performance has been validated on a proprietary database. The database contains paired ECG and heart sound recordings and echocardiograms from 3,456 unique subjects. The subject population was comprised of adults over the age of 18, with the median age being 64. 44.3% of subjects were female and 55.7% were male. The majority of subjects were White (58.2%), followed by Black or African American (21.6%), Asian (15.0%), American Indian or Alaska Native (0.8%), Native Hawaiian or Other Pacific Islander (0.1%), and Other (4.3%). No complications or adverse events were experienced during the use of the ELEFT device.

Ground truth for classification was obtained from gold standard echocardiogram. All subjects underwent echocardiography within a maximum of 7 days of the corresponding ECG and heart sound recordings. The subject's true ejection fraction was measured by the echocardiogram machine's integrated cardiac quantification software at the time of the echocardiogram and then overread by a board-certified cardiologist. Ejection fraction status was then assigned by categorizing the subject's measured ejection fraction into Low EF (≤40%) or Normal EF (> 40%).

Based on these two categories, 9.9% of recordings came from subjects with confirmed Low EF and 90.1% of recordings came from subjects with confirmed Normal EF. Of note, 307 recordings of the total 3,456 recordings were excluded from the performance analysis as a result of poor ECG quality.

The following table (Table 2) demonstrates the results of the primary performance analysis (Low EF Detection):

	Sensitivity (%)	**Specificity (%)**
Low EF Detection	74.7 (95% CI: 69.4-79.6)	77.5 (95% CI: 75.9-79.0)

Table 2: Clinical Performance of ELEFT.

Additional analysis of validation data supports the safety and effectiveness of the device in the intended use population, including patients at risk of heart failure not diagnosed with coronary artery disease; diabetes mellitus; cardiomyopathy; hypertension; and obesity.

In addition to the above performance data, the below summarizes the patient demographics for the

training and test sets as well as subgroup analyses to demonstrate generalizability, safety and effectiveness of the tool across patient populations.

Summary-Level Descriptions of Patient Demographics for Training Dataset

Eight sites within the US (n = 7) and India (n = 1) contributed training data from 1,515 and 337 patients, respectively. The median age in the training dataset was 66 (IQR 51-75). 51.3% (951) of patients were male and 45.7% (847) were female, while gender was unknown for the remaining 2.9% (54). The majority of patients were White (1,089 [58.8%]), followed by Black or African American (65 [3.5%]), Asian (423 [22.9%]), American Indian or Alaska Native (2 [0.1%]), Other (24 [1.3%]), Native Hawaiian or Other Pacific Islander (3 [0.2%]), and Unknown (246 [13.3%]). A total of 201 cases of EF <40% were identified from the 1,852 patients (prevalence 10.9%).

Summary-Level Descriptions of Patient Demographics for Test Dataset

Five sites within the US (n = 4) and India (n = 1) contributed data from 2,960 and 496 patients, respectively. For the prevalence of heart failure risk factors, see Table 1. The median age in the sample was 64 (IQR 52-73), and 44.3% (1,530) of patients were female. The majority of patients were White (2,011[58.2%]), followed by Black or African American (748 [21.6%]), Asian (517 [15.0%]), American Indian or Alaska Native (28 [0.8%]), Other (147 [4.3]), and Native Hawaiian or Other Pacific Islander (5, 0.1%) and therefore representative of the intended use population.

In this sample, 307 records were excluded as a result of poor ECG quality, and a total of 341 cases of EF <40% were identified from 3,456 samples (prevalence 9.9%). ELEFT achieved a sensitivity of 74.7% (95%CI: 69.4-79.6), a specificity of 77.5% (95%CI: 75.9- 79.0), a positive predictive value (PPV) of 25.7% (95%CI: 22.8-28.7), and a negative predictive value (NPV) of 96.7% (95%CI: 95.9 to 97.4).

SUBGROUP ANALYSES

Subgroup assessments of diagnostic performance were conducted to determine if there was heterogeneity in device performance across patient demographics, including conduction disorders. The results are summarized in Table 3 below.

Subgroup	Results of Test Heterogeneity
Age	Age was stratified into four groups: 18-30, 31-50, 51-70, >70 years. While no significant differences in sensitivity were observed among the age groups, the specificity of tests for patients aged >70 years (70.7% [95%CI: 67.8-73.5]) showed a slightly lower value compared to those performed on patients aged 31-50 (80.9% [95%CI: 77.3-84.3]) and 51-70 (81.1% [95%CI: 78.8-83.2]). Elderly patients are more likely to have several cardiac comorbidities, potentially resulting in higher rates of false positives.
Biological sex	Specificity varied slightly across biological sex (male: 73.6% [95% CI: 71.3-75.8] vs female: 81.8% [95% CI: 79.7-83.9]. However, this may not reflect a true difference, as the values may be confounded by the higher prevalence of cardiac comorbidities in the male subgroup (15.6% vs. 11.5%).
Body-Mass-Index (BMI)	BMI was stratified into six categories: <18.5, 18.5-24, 25-29, 30-34, 35-39, >=40 kg/m2. No significant differences were observed.
Race/ethnicity	No significant differences were observed.
Conduction disorders	In patients with pacemakers or cardiac comorbidities (e.g., atrial fibrillation, left bundle branch block, wide QRS complex [>120ms]), there was an overall trend toward increased sensitivity, however this was not significant. Specificity, conversely, was lower for patients with the above comorbidities. These comorbidities are known to cause variations in ECG morphology, resulting in higher rates of false positives in these subgroups.

Table 3: Clinical Performance in Pre-Specified Subgroup Analyses

CONCLUSIONS

The Eko Low Ejection Fraction Tool (ELEFT) has the same intended use and similar technological characteristics as the Anumana Low Ejection Fraction AI-ECG Algorithm . Differences in technological characteristics have been evaluated through performance testing has shown that the minor technological differences between ELEFT and the predicate device raise no new issues of safety or effectiveness. Bench and clinical data demonstrate that the ELEFT is substantially equivalent to the Anumana Low Ejection Fraction AI-ECG Algorithm .