eko.ai Pte. Ltd. d/b/a Us2.ai
% Jared Seehafer
Regulatory Consultant
Enzyme Corporation
611 Gateway Blvd., Suite 120
SOUTH SAN FRANCISCO CA 94080

July 27, 2021

Re: K210791
Trade/Device Name: Us2.v1
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: QIH
Dated: June 17, 2021
Received: June 24, 2021

Dear Jared Seehafer:

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,

For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and 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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K210791

Device Name
Us2.v1

Indications for Use *(Describe)*
Us2.v1 is a fully automated software platform that processes, analyses and makes measurements on acquired transthoracic cardiac ultrasound images, automatically producing a full report with measurements of several key cardiac structural and functional parameters. The data produced by this software is intended to be used to support qualified cardiologists or licensed primary care providers for clinical decision-making. Us2.v1 is indicated for use in adult patients. Us2.v1 has not been validated for the assessment of congenital heart disease, valve disease, pericardial disease, and/or intra-cardiac lesions (e.g. tumours, thrombi).

Please note the following limitations:
- Poor image capture will lead to poor annotations and subsequent measurements. Multiple image quality algorithms are used to filter out images of poor quality.
- Our software complements good patient care and does not exempt the user from the responsibility to provide supervision, clinically review the patient, and make appropriate clinical decisions.
- If no gender is present, female referenced guideline values will be used for conclusions.
- If Body Surface Area (BSA) is not present, indexed values cannot be provided.
- During image acquisition, inappropriate use of the echo machine, use of non-cardiac ultrasound probes, use of suboptimal settings (e.g. gain, contrast, depth), or lack of electrocardiogram capture may lead to lower accuracy of the software.

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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5 510(k) Summary

Table 5-1. Subject Device Overview.

Submission Number:	K210791
Submitter's Name:	Eko.ai Pte. Ltd. (d/b/a Us2.ai)
Address:	2 College Road, #02-00, Singapore 169850
Contact Person:	Jared Seehafer
Title:	Regulatory Consultant
Telephone Number:	415-857-9554
Fax Number:	415-367-1279
Email:	jared@enzyme.com
Date Summary Prepared:	July 15, 2021
Device Proprietary Name:	Us2.v1
Model Number:	V 1.0.0
Common Name:	Us2.v1
Regulation Number:	21 CFR 892.2050
Regulation Name:	System, Image Processing, Radiological
Product Code:	QIH
Device Class:	Class II
Predicate Device	Trade name: EchoMD Automated Ejection Fraction Software Manufacturer: Bay Labs, Inc. (now known as Caption Health, Inc.) 290 King Street San Francisco, CA 94107 Regulation Number: 21 CFR 892.2050 Regulation Name: System, Image Processing, Radiological Device Class: Class II Product Code: LLZ 510(k) Number: K173780 510(k) Clearance Date: June 14, 2018

5.1 Device Description

Us2.v1 is an image post-processing analysis software device used for viewing and quantifying cardiovascular ultrasound images in DICOM format. The device is intended to aid diagnostic review and analysis of echocardiographic data, patient record management and reporting.

The software provides an interface for a skilled sonographer to perform the necessary markup on the echocardiographic image prior to review by the prescribing physician. The markup includes: the cardiac segments captured, measurements of distance, time, area and blood flow, quantitative analysis of cardiac function, and a summary report.

The software allows the sonographer to enter their markup manually. It also provides automated markup and analysis, which the sonographer may choose to accept outright, to accept partially and modify, or to reject and ignore. Machine learning based view classification and border detection form the basis for this automated analysis. Additionally, the software has features for organizing, displaying and comparing to reference guidelines the quantitative data from cardiovascular images acquired from ultrasound scanners.

5.2 Indications for Use

Us2.v1 is a software platform that automatically processes, analyses and makes measurements on acquired transthoracic cardiac ultrasound images, producing a full report with measurements of several key cardiac structural and functional parameters. The data produced by this software is intended to be used to support qualified cardiologists or licensed primary care providers for clinical decision-making based on DICOM images produced by FDA approved ultrasound devices. Us2.v1 is indicated for use in adult patients. Us2.v1 has not been validated for the assessment of congenital heart disease, valve disease, pericardial disease, and/or intra-cardiac lesions (e.g. tumours, thrombi).

Please note the following limitations:

- Poor image capture will lead to poor annotations and subsequent measurements. Multiple image quality algorithms are used to filter out images of poor quality.
- Our software complements good patient care and does not exempt the user from the responsibility to provide supervision, clinically review the patient, and make appropriate clinical decisions.
- If no gender is present, female referenced guideline values will be used for conclusions.
- If Body Surface Area (BSA) is not present, indexed values cannot be provided.
- During image acquisition, inappropriate use of the echo machine, use of non-cardiac ultrasound probes, use of suboptimal settings (e.g. gain, contrast, depth), or lack of electrocardiogram capture may lead to lower accuracy of the software.

5.3 Summary of Technological Characteristics Comparison

Table 5-2 shows the similarities and differences between the technological characteristics of the two products. Testing demonstrates that the differences do not raise new questions of safety or effectiveness.

Table 5-2. Summary of Technological Characteristics Comparison.

Topic	**Predicate Device**	**Subject Device**
Physical Characteristics	Software package that operates utilizing off-the-shelf hardware	Same
DICOM Standard Compliance	The software processes DICOM compliant image data	Same
Modalities	Cardiac echocardiogram	Same
User Interface	The software is designed for use on a personal computer that has been received images from a compatible PACS	Same
Automation level	Fully automated, including clip selection	Same
User confirmation/ rejection of result	Yes	Yes
Manual editing of automated result by user	Yes (on PACS workstation)	Yes (in application)
Automated calculations	Ejection Fraction	**Region** / **Measurement** LV / DecT LV / MV-A LV / MV-Adur LV / MV-E LV / e' lateral LV / e' septal LV / a' lateral LV / a' septal LV / s' lateral LV / s' septal LV / LVEDV MOD biplane LV / LVEF MOD biplane LV / LVESV MOD biplane LV / LVSV MOD biplane LV / IVSd LV / LVIDd LV / LVIDs LV / LVPWd LV / E/e' mean RV / RVIDd LA / LAESV MOD biplane RA / Raa TrV / TR Vmax

5.4 Performance Data

Us2.v1 was developed and tested in accordance with Us2.ai's Design Control processes. The device has been subject to extensive safety and performance testing. Non-clinical verification and validationtest results established that the device meets its design requirements and intended use. Specifically, software verification was conducted at unit, module, and system integration levels. Risk managementanalysis generated multiple risk mitigation measures and verification activities. A Cybersecurity Analysis and data security testing were conducted to verify that data and patient protected health information security measures are included in the design of the software. A Human Factors/Usability Engineering study performed according to the principles of AAMI/ANSI HE75 was performed to validate device's usability within the intended user population.

A formal retrospective non-interventional validation study was conducted using 600 previously-acquired echocardiograms to evaluate the performance of the device for each claimed measurement. The patient dataset was constructed to provide a balanced range of gender and body mass index levels. A blinded, anonymized series of 600 unique echocardiographic studies was selected for analysis. Of these, 421 are samples of patients with heart failure with reduced ejection fraction. The remaining 179 examinations were from normal subjects. Both cohorts of subjects were selected fromsets of previously annotated and overread studies with robust inclusion criteria (see below).

Additional demographic information and vital signs at the time of examination are available in Table 1.

Two subject cohorts were used for analysis across 600 studies:

- HFrEF Subjects: *421 studies*
- Normal Subjects*: 179 studies*

Inclusion criteria were:

<u>HFrEF Subjects</u>

Subjects eligible for inclusion in this study met all of the following criteria at screening:

1. Written informed consent for the original study.
2. Men and women ≥ 18 years of age.
3. HFrEF subjects (heart failure with LVEF < 40% determined at the site)
4. NYHA Functional class II-IV.

<u>Normal Subjects</u>

Subjects eligible for inclusion in this study met all of the following criteria at screening:

1. Written informed consent for obtained.
2. Males and females (of non-childbearing potential) between 18 and 55 years of age,inclusive

3. Body weight > 55.0 kg and body mass index within 18.0 to 32.0 kg/m2, inclusive
4. In good health, in the opinion of the Investigator, as determined by the following:
    a. A physical examination at screening and medical history with no clinically significant abnormalities
    b. Not taking medications for the treatment of any chronic or episodic medicaldisease or condition
    c. Vital signs within the ranges below measured while the subject is supine after 3 minutes rest. May re-check vital signs twice at screening.
        * heart rate 40-90 beats per minute; systolic blood pressure (BP) 100-140 mmHg; diastolic BP 50-95 mmHg; respiration rate <25 breaths per minute; oxygen saturation: 95-100%

5. Acoustic windows adequate for accurate transthoracic echocardiograms, confirmed by the echocardiography core laboratory
6. Normal cardiac structure and function, as determined by the echocardiography corelaboratory, or if abnormalities are present, they are deemed not clinically significant LVEF > 55%
7. Normal electrocardiogram (ECG) or, if abnormalities are present, they are deemed notclinically significant by the Investigator

Table 1. Demographics of Cohort

	Normal Cohort	**HFrEF Cohort**
Age	40.0 (± 7.5) years	64.3 (± 12.5) years
% Male	72.6%	67.4%
Height	168.1 (± 9.4) cm	172.2 (± 10.3) cm
Weight	76.6 (± 9.2) kg	93.4 (± 24.9) kg
Heart Rate	62.7 (± 7.1) bpm	72.2 (± 11.9) bpm
Systolic Blood Pressure	112.0 (± 9.7) mmHg	124.6 (± 18.1) mmHg
Diastolic Blood Pressure	71.2 (± 7.9) mmHg	74.1 (± 11.5) mmHg

Test datasets were strictly segregated from algorithm training datasets. The primary performance metric is the reference-scaled individual equivalence coefficient (IEC, Barnhart, 2007) across three human readers and one automated read performed by Us2.v1.

We define our success criterion as a non-inferiority margin, $\Delta = 0.25$, such that Us2.v1 is deemed interchangeable with the reference if IEC + 1.96*SD(IEC) < Δ. Compared to reference standard echocardiographic human measurements made in triplicate by the independent Cardiovascular Imaging Core Laboratory at Brigham and Women's Hospital, the 95% confidence intervals of automated Us2.v1 measurements all fell below the pre-specifiednon-inferiority margin of 0.25 for IEC.

Based on the performance as documented in the sum of this testing, the Us2.v1 device has a safety and effectiveness profile that is similar to the predicate EchoMD Automated Ejection Fraction Software device.

5.5 Substantial Equivalence Conclusion

Us2.v1 is an image processing software which has similar intended use and indications for use statement as the predicate device. The two devices have similar technological characteristics: both use machine learning algorithms to automate the measurement of transthoracic cardiac images. Though the subject device provides more measurements than the predicate, this does not in and of itself produce different questions of safety and effectiveness. This 510(k) submission includes information on the Us2.v1 technological characteristics, as well as performance data and verification and validation activities demonstrating that Us2.v1 is as safe and effective as the predicate, and does not raise different questions of safety and effectiveness.