December 18, 2020

Ultromics Ltd.
% Mr. Neela Hassanali
Head of Regulatory
4630 Kingsgate, Cascade Way, Oxford Business Park South
Oxford, Oxfordshire OX4 2SU
UNITED KINGDOM

Re: K201555
Trade/Device Name: EchoGo Pro
Regulation Number: 21 CFR 892.2060
Regulation Name: Radiological computer-assisted diagnostic software for lesions suspicious of cancer
Regulatory Class: Class II
Product Code: POK
Dated: November 8, 2020
Received: November 10, 2020

Dear Mr. Hassanali:

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,

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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K201555

Device Name
EchoGo Pro

Indications for Use *(Describe)*

EchoGo Pro v1.0.2 is a machine learning-based decision support system, indicated as an adjunct to diagnostic stress echocardiography for patients undergoing assessment for coronary artery disease (CAD). When utilized by an interpreting physician, this device provides information that may be useful in rendering an accurate diagnosis. Patient management decisions should not be made solely on the results of the EchoGo Pro v1.0.2 analysis. EchoGo Pro v1.0.2 is to be used with stress echo exam protocols that contain A2C, A4C and mid-ventricular short-axis views at rest and at peak stress. EchoGo Pro vl.0.2 is not intended for the assessment of mild or moderate myocardial ischemia, or localization of coronary artery disease, or for the assessment of myocardial perfusion, myocardial viability or valve disease.

Limitations: EchoGo Pro v1.0.2 has not been validated on patients who underwent previous coronary artery bypass graft (CABG) surgery

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.

6. 510(K) SUMMARY

The Company's 510(k) Summary is provided on the following pages.

1. Submitter

Company & Address:	Ultromics Ltd 4630 Kingsgate Cascade Way Oxford Business Park South Oxford, OX4 2SU 203-906-4644
Contact Person:	Neelam Hassanali
Contact Email:	neelam.hasssanali@ultromics.com

Date Prepared:	June 8, 2020
Date Updated:	December 16, 2020

2. Device

Name of Device:	EchoGo Pro
Common or Usual Name:	Computer-Assisted Diagnostic Software (CADx)
Classification Name:	Computer-Assisted Diagnostic Software (CADx) for lesions suspicious for cancer
Regulation:	21 CFR §892.2060
Regulatory Class:	II
Product Code:	POK

3. Predicate Device

Koios Medical, Inc. Koios DS For Breast device (K190442)

The predicate device has not been subject to a design-related recall.

4. Device Description

EchoGo Pro v1.0.2 is a standalone software application that utilizes anonymized DICOM 3.0 compliant stress echo (SE) datasets to provide a categorical assessment as to whether the data are suggestive of a higher or lower possibility of significant CAD. The software automatically registers images, and segments and analyses selected regions of interest (ROI). EchoGo Pro v1.0.2 utilizes standard clinical SE protocols that provide apical 2 chamber, 4 chamber and parasternal short axis (SAX) views.

Ultrasound images are acquired from a third-party acquisition device. The incoming DICOM study is checked for consistency and completeness, i.e. whether all required views labels are present in

the DICOM metadata. Once the technical QC has been performed on the DICOM datasets, the algorithm for automated contour detection of the endocardium of the LV is applied and presented for review and approval by trained Operators. An auto-contouring algorithm places a trace around the LV that sufficiently captures the LV shape. Outlining is detected for all frames in between and including end-systole (ES) and end-diastole (ED) for AP2, AP4, and mid-ventricular short axis (SAX) views of the LV at both rest and peak stress. Trained operators review and approve of the contour traces. The approved contour traces are used in calculations for geometric parameters.

Geometric parameters are calculated from the approved contours and are fed into a fixed classification model that has been previously trained on datasets with known outcomes. The output of the pre-trained model generates a report which contains a categorical assessment as to whether the data are consistent with significant CAD or not. Significant CAD as determined by EchoGo Pro, based on LV segmentation (ROI) analysis, and was defined as ≥70% stenosis in the proximal to mid LAD, proximal left circumflex or proximal to mid RCA as measured by invasive angiography performed within 6 months of stress echocardiogram.

5. Indications for Use

EchoGo Pro v1.0.2 is a machine learning-based decision support system, indicated as an adjunct to diagnostic stress echocardiography for patients undergoing assessment for coronary artery disease (CAD). When utilized by an interpreting physician, this device provides information that may be useful in rendering an accurate diagnosis. Patient management decisions should not be made solely on the results of the EchoGo Pro v1.0.2 analysis. EchoGo Pro v1.0.2 is to be used with stress echo exam protocols that contain A2C, A4C and mid-ventricular short-axis views at rest and at peak stress. EchoGo Pro vl.0.2 is not intended for the assessment of mild or moderate myocardial ischemia, or localization of coronary artery disease, or for the assessment of myocardial perfusion, myocardial viability or valve disease.

Limitations: EchoGo Pro v1.0.2 has not been validated on patients who underwent previous coronary artery bypass graft (CABG) surgery."

6. Comparison of Intended Use

The intended use of the EchoGo Pro and the predicate, Koios DS For Breast device (K190442), is to act as a diagnostic aid using machine learning to assist trained interpreting physicians in analyzing ultrasound images and characterize ultrasound image features for given regions of interest (ROIs) to generate a categorical output. Both devices:

- are used as an aid to diagnosis (not for primary diagnosis).
- are intended for patients being referred for further diagnostic ultrasound examination.

- requires a user to select multiple ROIs, from multiple orthogonal views, that represent a single anatomical feature to be processed.
- are intended to help trained interpreting physicians improve their overall accuracy as well as reduce inter-operator variability.
- intended use population includes patients presenting with disease through any form of imaging or physical examination resulting in a referral for diagnostic ultrasound - thus covering diagnostic imaging workup or the evaluation of known disease.

The indications for use for the EchoGo Pro and Koios DS for Breast differ in that the EchoGo Pro is indicated for patients undergoing assessment for coronary artery disease, whereas the Koios DS for Breast is indicated for patients with soft tissue breast lesions examination. As such, the subject device provides a categorical output related to coronary artery disease whereas the predicate device provides a categorical output that aligns to BI-RADS and auto-classified shape and orientation.

The difference in Indications for Use statement does not affect the safety and effectiveness of the device when used as labeled. Both the subject and predicate devices have the same intended use for characterizing image features for given ROIs to generate categorical output that is used as an aid to diagnosis.

7. Comparison of Technological Characteristics with the Predicate Device

The technical principle of both the EchoGo Pro and the predicate is characterization of ultrasound image features with ROIs to generate a categorical output. The results of the output are used as an aid to diagnosis. Both devices provide computer analytics based on morphological and enhancement characteristics that the predicate device refers to as imaging features that are then synthesized by an artificial intelligence (machine learning) algorithm into a categorical output. At a high level, the subject and predicate devices are based on the following same technological elements:

- Generation of a categorical output that analyzes imaging features relative to a dataset of known ground truth
- Software as a medical device (SaMD)
- Use of artificial intelligence / Machine Learning-Based Algorithm
- Characterization of image features with ROIs to generate categorical output
- Ultrasound modality for analysis
- Input is images provided in a DICOM format
- Images can be viewed
- Selection of multiple views for processing

- Allow for ROIs to be selected in multiple views for the assessment of one anatomical feature
- Assess views that are orthogonal
- Operates on a Windows platform
- Operates on off the shelf hardware
- Output is a report which is returned to the physician for review
- Output of the system is to be used as a diagnostic aid

The following technological differences exist between the subject and predicate devices:

- ROI are selected automatically by the subject device and by the user in the predicate device.
- The output of the subject pre-trained model gives a categorical assessment as to whether the data are suggestive of a higher or lower possibility of significant coronary artery disease or not, whereas the predicate device uses a pre-trained model to provide an indication of the probability as to whether the data are indicative of cancer or not.
- While both devices generate a categorical output that analyzes imaging features relative to a dataset of known ground truth, the predicate device generates a four-level and the subject device generates a two-level output. The predicate device provides four categorical outputs: Benign, Probably Benign, Suspicious, Probably Malignant vs. two for the subject device: Stress Echocardiogram ROIs are suggestive of a higher possibility of significant CAD, Stress Echocardiogram ROIs are suggestive of a lower possibility of significant CAD. The predicate device also provides output related to shape, orientation, and confidence level. The subject device does not provide this information on the report; however, the user can see shape and orientation of the image while using the device.

8. Performance Data

Software Verification and Validation Testing

Software verification and validation testing were conducted, and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "*Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices*." The software for this device is considered as a "moderate" level of concern, since a failure or latent design flaw could indirectly result in minor injury to the patient or operator through incorrect or delayed information or through the action of a care provider.

Performance / Clinical Testing

The objective of performance testing was to assess the clinical indication and substantial equivalence of EchoGo Pro by demonstrating:

- The difference between the diagnostic performance of readers when interpreting ultrasound studies with and without the assistance of EchoGo Pro v1.0.2 is equivalent or better than that of the predicate device.
- The difference between inter-operator agreement when interpreting ultrasound studies with and without the assistance of EchoGo Pro v1.0.2. is equivalent or better than that of the predicate device.

Per the primary endpoint of the study, ROC curves were generated and analyzed. All AUROC curves were computed via the trapezoidal approximation. Based on the standard error measurements, the error was propagated to estimate the mean performance interface and 95% confidence interval. This was found to be 0.054 (95%CI 0.032, 0.077) at p = 0.02, satisfying the acceptance criteria for the primary endpoint. The increase in reader performance with EchoGo Pro v1.0.2 exceeded the mean reader improvement in the AUROC reported for Koios DS in K190442, which was 0.034. The system achieved a native system performance of 0.927 AUROC, with specificity of 0.927 (95% CI 0.878, 0.976) and a sensitivity of 0.844 (95% CI 0.739, 0.950), greater than the native system performance reported for the predicate device (K190442) of 0.882.

To characterize the effect of the EchoGo Pro v1.0.2 (USE + EGP) system on inter-clinician variability, the Kendall Tau-B correlation coefficient was computed in a pairwise manner for all readers. The metric was > 0 for all reader pairs. The standard error for USE + EGP and USE Alone was computed to assess if the shifts in the metric were significant. The average Kendall Tau-B of USE Alone was 0.58 (0.48, 0.69) and the average Kendall Tau-B of USE + EGP was 0.82 (0.72, 0.93) with 95% CI demonstrating a significant increase in the metric (p<0.001). The increase in reader agreement with EchoGo Pro v1.0.2 exceeded the mean Kendall Tau-B improvement reported for Koios DS in K190442, which was 0.1393.

Based on the substantial equivalence evaluation, which is derived from the nonclinical and clinical tests demonstrate that the device is as safe, as effective, and performs as well as or better than the legally marketed device predicate, we have determined that the EchoGo Pro is substantially equivalent to the predicate device.

9. Conclusions

EchoGo Pro is as safe and effective as the Koios DS For Breast device. EchoGo Pro has the same intended uses and similar technological characteristics and principles of operation as its predicate device. The minor differences in indications do not alter the intended use of the device and do not affect its safety and effectiveness when used as labeled. In addition, the minor technological differences between the EchoGo Pro and its predicate devices raise no new issues of safety or effectiveness. Performance data, including software verification and validation and performance

testing demonstrate that the EchoGo Pro is as safe and effective as the Koios DS For Breast device, and therefore substantially equivalent.