Circle Cardiovascular Imaging, Inc.
℅ Sydney Toutant
Regulatory Affairs Lead
Suite 1100 - 800 5th Ave. SW
Calgary, Alberta T2P 3T6
CANADA

7/28/2022

Re: K213998
Trade/Device Name: cvi42 Auto Imaging Software Application
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: QIH, LLZ
Dated: June 27, 2022
Received: June 28, 2022

Dear Sydney Toutant:

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,

Jessica Lamb, Ph.D.
Assistant Director
Imaging Software Team
DHT8B: Division of Radiological Imaging Devices and Electronic Products
OHT8: Office of 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)*
K213998

Device Name
cvi42 Auto Imaging Software Application

Indications for Use *(Describe)*
cvi42 Auto is intended to be used for viewing, post-processing, qualitative and quantitative evaluation of cardiovascular magnetic resonance (MR) and computed tomography (CT) images in a Digital Imaging and Communications in Medicine (DICOM) Standard format.

It enables a set of tools to assist physicians in qualitative assessment of cardiac images and quantitative measurements of the heart and adjacent vessels; perform calcium scoring; and to confirm the presence or absence of physician-identified lesion in blood vessels.

The target population for cvi42 Auto's manual workflows is not restricted; however, cvi42 Auto's semi-automated machine learning algorithms are intended for an adult population.

cvi42 Auto shall be used only for cardiac images acquired from an MR or CT scanner. It shall be used by qualified medical professionals, experienced in examining and evaluating cardiovascular MR or CT images, for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process.

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.

K213998 - cvi42 Auto 510(k) Summary

The following 510(k) summary of safety and effectiveness information is submitted in accordance with the requirements of the Safe Medical Device Act 1990 and 21 CFR 807.92(c).

I. SUBMITTER

Submitter's Name:	Circle Cardiovascular Imaging Inc.
Address:	Suite 1100 – 800 5th Ave SW, Calgary, AB, Canada, T2P 3T6
Date Prepared:	July 25 2022
Telephone Number:	+1 587 747 4692
Contact Person:	Sydney Toutant
Email:	sydney.toutant@circlecvi.com

II. DEVICE

Name of the Device:	cvi42 Auto Imaging Software Application
Short Brand Name:	cvi42 Auto
Common or Usual Name:	Automated Radiological Image Processing System
Classification Name:	Medical image management and processing system
Proposed Classification:	Device Class: II Primary Product Code: QIH Secondary Product Code: LLZ Regulation Number: 21 CFR 892.2050

III. PREDICATE DEVICES

The primary predicate is cmr[42] manufactured by Circle Cardiovascular Imaging Inc. under K082628. cvi42, manufactured by Circle Cardiovascular Imaging Inc. under K141480, is used as a secondary predicate device and ct[42], manufactured by Circle Cardiovascular Imaging Inc. under K111373, is used as a tertiary predicate device. The predicate devices have not been subject to a design-related recall.

IV. DEVICE DESCRIPTION

cvi42 Auto is a software as a medical device (SaMD) that is intended for evaluating CT and MR images of the cardiovascular system. Combining digital image processing, visualization, quantification, and reporting tools, cvi42 Auto device is designed to support the physician in confirming the presence or absence of physician-identified lesion in blood vessels and evaluation, documentation and follow up of any such lesions.

cvi42 Auto uses machine learning techniques to aid in semi-automatic contouring of regions of interest of cardiac magnetic resonance (MR) or computed tomography (CT) images as follows:

1. **Cardiac Function:** semi-automatic contouring of the four heart chambers (including left ventricle, left atrium, right ventricle, right atrium) in MR images.
2. **Calcium Assessment:** using pixel intensity technique, identify calcified plaque in major coronary arteries in non-contrast enhanced CT images.
3. **Coronary Analysis:** semi-automatic placement of centerline in coronary vessels to visualize the coronary arteries and assess stenosis in non-contrast enhanced CT images.

The data used to train these machine learning algorithms were sourced from multiple clinical sites from urban centers and from different countries. When selecting data for training, the importance of model generalization was considered and data was selected such that a good distribution of patient demographics, scanner, and image parameters were represented. The separation into training versus validation datasets is made on the study level to ensure no overlap between the two sets. As such, different scans from the same study were not split between the training and validation datasets. None of the cases used for model validation were used for training the machine learning models.

cvi42 Auto software has a graphical user interface which allows users to analyze cardiac images qualitatively and quantitatively for volume/mass, function and signal intensity changes including a reporting function.

The device can be integrated into a hospital, private practice environment, or medical research institution and provides clinical diagnosis decision support tools for the cardiovascular MR and CT technique.

Additionally, the software is designed to generate 3D view of the heart in CT images for qualitative assessment of the coronary artery. No quantitative assessment can be made from the 3D image.

The software does not interface directly with any data collection equipment; instead, the software uploads data files previously generated by such equipment. Its functionality is independent of the type of vendor acquisition equipment. The analysis results are available on-screen and can be saved within the software for future review.

V. INDICATIONS FOR USE

cvi42 Auto is intended to be used for viewing, post-processing, qualitative and quantitative evaluation of cardiovascular magnetic resonance (MR) and computed tomography (CT) images in a Digital Imaging and Communications in Medicine (DICOM) Standard format.

It enables a set of tools to assist physicians in qualitative assessment of cardiac images and quantitative measurements of the heart and adjacent vessels; perform calcium scoring; and to confirm the presence or absence of physician-identified lesion in blood vessels.

The target population for cvi42 Auto's manual workflows is not restricted; however, cvi42 Auto's semi-automated machine learning algorithms are intended for an adult population.

cvi42 Auto shall be used only for cardiac images acquired from an MR or CT scanner. It shall be used by qualified medical professionals, experienced in examining and evaluating cardiovascular MR or CT images, for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process.

VI. COMPARISON WITH PREDICATE DEVICES

The detailed analysis of the subject device and the primary and secondary predicate devices (shown in **Table 1** and **Table 2**) demonstrates that the subject device is substantially equivalent in indications for use, intended use, technological characteristics, functionality, and operating principles with the primary predicate (K082628) and substantially equivalent in intended use and technological characteristics with the secondary predicate (K141480) and tertiary predicate (K111373). Of the three characteristics (technical, biological, and clinical) required for the demonstration of equivalence, biological characteristics are not applicable since the subject device and the predicate devices are all software as a medical device applications with no tangible component interfacing with the body.

Table 1. Comparison to the predicate devices.

	Subject Device *cvi42 Auto (K213998)* Manufactured by Circle	**Primary Predicate** *cmr^{42} (K082628)* Manufactured by Circle	**Secondary Predicate** *cvi42 (K141480)* Manufactured by Circle	**Tertiary Predicate** *ct^{42} (K111373)* Manufactured by Circle
Intended Use	Viewing, post-processing, qualitative and quantitative evaluation of blood vessels and cardiovascular MR and CT images in DICOM format.	Viewing, post-processing, qualitative and quantitative evaluation of cardiovascular MR images in DICOM format.	Viewing, post-processing, qualitative and quantitative evaluation of blood vessels and cardiovascular MR and CT images in DICOM format.	Viewing, post-processing, qualitative and quantitative evaluation of cardiovascular CT images in DICOM format.
Indications for Use	cvi42 Auto is intended to be used for viewing, post-processing, qualitative and quantitative evaluation of cardiovascular magnetic resonance (MR) and computed tomography (CT) images in a Digital Imaging and Communications in Medicine (DICOM) Standard format. It enables a set of tools to assist physicians in qualitative assessment of cardiac images and quantitative measurements of the heart and adjacent vessels; perform calcium scoring; and to confirm the presence or absence of physician-identified lesion in blood vessels. The target population for cvi42 Auto's manual workflows is not restricted; however, cvi42 Auto's semi-automated machine learning algorithms are intended for an adult population. cvi42 Auto shall be used only for cardiac images acquired from an MR or CT scanner. It shall be used by qualified medical professionals, experienced in examining and	cmr^{42} is intended to be used for viewing, post-processing and quantitative evaluation of cardiovascular magnetic resonance (MR) images in a Digital Imaging and Communications in Medicine (DICOM) Standard format. It enables; • Importing Cardiac MR Images in DICOM format • Supporting clinical diagnostics by qualitative analysis of the cardiac MR images using display functionality such as panning, windowing, zooming, navigation through series/slices and phases. • Supporting clinical diagnostics by quantitative measurement of the heart and adjacent vessels in cardiac MR images, specifically distance, area, volume and mass • Supporting clinical diagnostics by using area and volume measurements for measuring LV function and derived parameters cardiac output and cardiac index in long axis and short axis cardiac MR images. • Flow quantifications based on velocity encodes images	cvi42 vascular analysis add-on is an image analysis software package add-on for evaluating CT and MR images of blood vessels. Combining digital image processing and visualization tools such as multiplaner reconstruction (MPR), thin/think maximum intensity projection (MIP) thin and think, inverted MIP thin and think, volume rendering technique (VRT), curved planner reformation, processing tools such as bone removal (based on both single energy and dual energy) table removal and evaluation tools (vessel centerline calculation, lumen calculation, stenosis calculation) and reporting tools (lesion location, lesion characteristics) and key images), the software package is designed to support the physician in conforming the presence or absence of physician identified lesion in blood vessels and evaluation, documentation and follow up of any such lesions. It shall be used by qualified medical professionals, experienced in examining and evaluating cardiovascular CT or MR images,	ct^{42} is intended to be used for viewing, post-processing and quantitative evaluation of cardiovascular computed tomography (CT) images in a Digital Imaging and Communications in Medicine (DICOM) Standard format. It enables: • Importing Cardiac CT Images in DICOM format • Supporting clinical diagnostics by qualitative analysis of the cardiac CT images using display functionality such as panning, windowing, zooming, navigation through series/slices and phases, 3D reconstruction of images including multi-lanner reconstructions of the images. • Supporting clinical diagnostics by quantitative measurement of the heart and adjacent vessels in cardiac CT images, specifically distance, area, volume and mass • Supporting clinical diagnostics by using area and volume measurements for measuring LV function and derived parameters cardiac output and cardiac index in long axis and short axis cardiac CT images.

	Subject Device *cvi42 Auto (K213998)* Manufactured by Circle	**Primary Predicate** *cmr^{42} (K082628)* Manufactured by Circle	**Secondary Predicate** *cvi42 (K141480)* Manufactured by Circle	**Tertiary Predicate** *ct^{42} (K111373)* Manufactured by Circle
	evaluating cardiovascular MR or CT images, for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process.	It shall be used by qualified medical professionals, experienced in examining and evaluating cardiovascular MR images, for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process. cmr^{42} is a software application that can be used as a stand-alone product or in a networked environment. The target population for the cmr^{42} is not restricted, however the image acquisition by a cardiac magnetic resonance scanner may limit the use of the device for certain sectors of the general public. cmr^{42} shall not be used to view or analyze images of any part of the body except the cardiac magnetic resonance images acquired from a cardiovascular magnetic resonance scanner.	for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process. cvi42 is a software application that can be used as a stand-alone product or in a networked environment. The target population for the cvi42 is not restricted.	• Supporting clinical diagnostics by quantitative measurements of calcified plaques in the coronary arteries (calcium scoring), specifically Agatston and volume and mass calcium scores It shall be used by qualified medical professionals, experienced in examining and evaluating cardiovascular CT images, for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process. ct^{42} is a software application that can be used as a stand-alone product or in a networked environment. The target population for the ct^{42} is not restricted, however the image acquisition by a cardiac CT scanner may limit the use of the device for certain sectors of the general public. ct^{42} shall not be used to view or analyze images of any part of the body except the cardiac CT images acquired from a cardiovascular CT scanner.

Table 2. Feature comparison table of cvi42 Auto with the predicate devices.
Cells marked as N/A are features already supported by the primary predicate.

Feature	**Subject Device** *cvi42 Auto (K213998)* Manufactured by Circle	**Primary Predicate** *cmr^{42} (K082628)* Manufactured by Circle	**Secondary Predicate** *cvi42 (K141480)* Manufactured by Circle	**Tertiary Predicate** *ct42 (K111373)* Manufactured by Circle
Device Class	II	II	II	II
Device Classification	QIH, LLZ	LLZ	LLZ	LLZ
Regulation Name	Medical image management and processing system	Picture Archiving and Communications System	Picture Archiving and Communications System	Picture Archiving and Communications System
Regulation Number	21 CFR 892.2050	21 CFR 892.2050	21 CFR 892.2050	21 CFR 892.2050
Imaging Modalities	MR and CT	MR	MR and CT	CT
DICOM Compliant	Yes	Yes	N/A	N/A
Import and display MR/CT images	Yes	Yes (MR only)	Yes	Yes (CT only)
Post process CMR/CCT images	Yes	Yes (MR only)	Yes	Yes (CT only)
Images can be displayed by study and series	Yes	Yes	N/A	N/A
Store images	Yes	Yes	N/A	N/A
2D Imaging	Yes	Yes	N/A	N/A
3D Imaging	Yes	No	Yes	Yes
Multiplanar Reformat (MPR)	Yes	No	Yes	Yes
Navigation Tools	Panning, Windowing, Zooming Series/slices and phases	Panning, Windowing, Zooming Series/slices and phases	N/A	N/A
Measurements	Distance Perimeter Area Signal Intensity Volume	Distance Perimeter Area Signal Intensity Volume	N/A	N/A
Quantitative assessment of cardiac function	Manual segmentation, and semi-automatic segmentation using Machine Learning technique of four heart chambers in long and short-axis views	Manual segmentation of four heart chambers in long and short-axis views	Manual segmentation, and semi-automatic segmentation of four heart chambers in long and short-axis views	Manual segmentation, and semi-automatic segmentation of four heart chambers in short-axis views

Feature	**Subject Device** *cvi42 Auto (K213998)* Manufactured by Circle	**Primary Predicate** *cmr^{42} (K082628)* Manufactured by Circle	**Secondary Predicate** *cvi42 (K141480)* Manufactured by Circle	**Tertiary Predicate** *ct42 (K111373)* Manufactured by Circle
Centerline placement in coronary vessels	Manual and semi-automatic using Machine Learning technique	Manual	Manual and semi-automatic	Manual and semi-automatic
Calcium Scoring	Yes, using ML methodology	No	No	Yes, using non-ML methodology
Workstation operating system	macOS, Microsoft Windows	macOS, Microsoft Windows	macOS, Microsoft Windows	macOS, Microsoft Windows

VII. PERFORMANCE DATA AND TESTING

Performance testing was conducted to verify compliance with specified design requirements in accordance with ISO 13485:2016, IEC 62304:2015, ISO 14971:2019 and NEMA 3.1-3.20 (2016) DICOM standards.

Verification and validation testing were conducted to ensure specifications and performance of the device and were performed per the FDA Guidance documents *"Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices"* and *"Content of Premarket Submission for Management of Cybersecurity in Medical Devices".*

cvi42 Auto has been tested according to the specifications that are documented in a Master Software Test Plan. Testing is an integral part of Circle Cardiovascular Imaging Inc software development process as described in the company's product development process.

Validation of Machine Learning Derived Outputs

The machine learning algorithms of cvi42 Auto (MR-CMR Function, CT-Coronary, and CT-Calcium) have been trained and tested on images acquired from major vendors of MR and CT imaging devices. All data used for validation were not used during the development of the training algorithms.

Across all MR and CT machine manufacturers, n = 235 anonymized patient images were used for the validation of cvi42 Auto. This translates into 70 samples for Coronary Analysis, 102 samples for Calcium analysis, 63 samples for SAX Function contouring, 63 for each of 2-CV, 3-CV, and 4CV LAX function contouring, and 252 samples for Function Classification. Image information for all samples was anonymized and limited to ePHI-free DICOM headers. At least 50% of the data came from a U.S. population.

All performance testing results met Circle's pre-defined acceptance criteria.

- For CMR function analysis, the performance acceptance criteria were pre-defined to evaluate the performance of the ML model based on classification accuracy defined by true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN). Mean volume prediction error (Mean Absolute Error, or MAE) was also calculated. Series classification performance results were between 97 % - 100%. Volumetric MAE for SAX were between 7% - 10%, and volumetric MAE for LAX were between 5% - 9%.
- For Calcium analysis, the performance acceptance criteria were pre-defined to evaluate the performance of the ML model based on classification accuracy defined by TP, TN, FP, and FN. Classification performance results were between 86% - 99%.
- For Coronary analysis, the performance acceptance criteria were pre-defined to evaluate the centerline quality and performance (based on TP and FN), and success rate for relevant masks. Centerline performance results were between 82% - 94%. Mask performance results were between 98% - 100%.

VIII. CONCLUSIONS

The information submitted in this premarket notification, including the performance testing and predicate device comparisons, supports the safety and effectiveness of cvi42 Auto as compared to the predicate devices when used for the defined intended use.