Circle Cardiovascular Imaging Inc.
Omar Naimi
Regulatory Affairs Analyst
Suite 1800, 707 8 Avenue SW
Calgary, AB T2P 1H5
Canada

October 15, 2024

Re: K242781
Trade/Device Name: cvi42 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: September 13, 2024
Received: September 16, 2024

Dear Omar Naimi:

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.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

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,

Jessica Lamb, Ph.D.
Assistant Director
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: 07/31/2026
*See PRA Statement below.*

Submission Number *(if known)*

K242781

Device Name

cvi42 Software Application

Indications for Use *(Describe)*

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

It enables:
• Importing cardiac MR & CT Images in DICOM format.
• Supporting clinical diagnostics by qualitative analysis of cardiac MR & CT images using display functionality such as panning, windowing, zooming, navigation through series/slices and phases, 3D reconstruction of images including multiplanar reconstructions of the images.
• Supporting clinical diagnostics by quantitative measurement of the heart and adjacent vessels in cardiac MR & CT images, specifically signal intensity, distance, area, volume, and mass.
• Supporting clinical diagnostics by using area and volume for measuring cardiac function and derived parameters cardiac output and cardiac index in long axis and short axis cardiac MR & CT images.
• Flow quantifications based on velocity encoded cardiac MR images (including two and four dimensional flow analysis).
• Strain analysis of cardiac MR images by providing measurements of 2D LV myocardial function (displacement, velocity, strain, strain rate, time to peak, and torsion).
• Supporting clinical diagnostics of cardiac CT images including quantitative measurements of calcified plaques in the coronary arteries (calcium scoring), specifically Agatston and volume and mass calcium scores, visualization and quantitative measurement of heart structures including coronaries, femoral, aortic, and mitral valves.
• Evaluating CT and MR images of blood vessels. Combining digital image processing and visualization tools such as multiplanar reconstruction (MPR), thin/thick maximum intensity projection (MIP), inverted MIP thin/thick, volume rendering technique (VRT), curved planar reformation (CPR), 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 confirming the presence or absence of physician identified lesion in blood vessels and evaluation, documentation and follow up of any such lesions.

cvi42 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. cvi42 is a software application that can be used as a stand-alone product or in a networked environment.

The target population for cvi42 and its manual workflows is not restricted; however, cvi42's semi-automated machine learning algorithms, included in the MR Function and CORE CT modules, are intended for an adult population. Further, image acquisition by a cardiac MR or CT scanner may limit the use of the software for certain sectors of the general public.

cvi42 shall not be used to view or analyze images of any part of the body except the cardiac images acquired from a cardiovascular magnetic resonance or computed tomography scanner.

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.**

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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# cvi42 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 1800 – 707 8th Ave SW, Calgary, AB, Canada, T2P 1H5 |
| **Date Prepared:** | October 11 2024 |
| **Telephone Number**: | +1 587-686-0784 |
| **Contact Person :** | Omar Naimi |
| **Email:** | omar.naimi@circlecvi.com |


## II. DEVICE

| | |
|---|---|
| **510(k):** | K242781 |
| **Name of the Device:** | cvi42 Software Application |
| **Short Brand Name:** | cvi42 |
| **Common or Usual Name:** | Automated Radiological Image Processing Software |
| **Classification Name:** | Medical image management and processing system |
| **Proposed Classification:** | Device Class: II<br>Product Codes: QIH, LLZ<br>Regulation Number: 21 CFR 892.2050 |

## III. PREDICATE DEVICE

The primary predicate is cmr[42] under K082628, and the additional predicates are ct[42] under K111373, cvi42 vascular add-on under K141480, cvi42 Auto under K213998, Strain Module under 232661, and CT Function under 241038. Each of the predicate devices are manufactured by Circle Cardiovascular Imaging Inc.

The predicate devices have not been subject to a design-related recall.

## IV. DEVICE DESCRIPTION

cvi42 Software Application ("cvi42") 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 is designed to support physicians in the evaluation and analysis of cardiovascular imaging studies.

cvi42 uses machine learning techniques to aid in semi-automatic contouring of regions of interest in cardiac MR or 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 has a graphical user interface which allows users to analyze cardiac MR & CT images qualitatively and quantitatively.

cvi42 accepts uploaded data files previously acquired by MR or CT scanners or other data collection equipment but does not interface directly with such equipment. Its functionality is independent of the type of vender acquisition equipment. The analysis results are available on-screen and can be saved with the software for future review.

*Table 1. Measurements in cvi42.*

| Measurement [units] | Description | Application |
|---|---|---|
| Distance [mm] | Length between two points, for both curved lines (splines) and straight lines, including the diameter (including min, max, average) resulting from closed splines and depth | Diameter & depth of cardiovascular structures of interest |
| Perimeter [mm] | The perimeter of a contour (closed spline) | Perimeter of cardiovascular structures of interest |
| Area [$cm^2$] | The area within contour(s) | Area of cardiovascular structures of interest |
| Signal intensity [HU] (modality CT) / Intensity [unitless] (modality MR) | Modality CT: Hounsfield value (in Hounsfield Units, HU) of the underlying pixels<br><br>Modality MR: Intensity / shade of grey (high, intermediate, low) of underlying pixels | Intensity of pixels in cardiovascular structures of interest |
| Volume [$mm^3$ or mL] | The volume within contour(s) | Volume of cardiovascular structures of interest |
| Coordinates [mm, mm, mm] | Location in the x-, y-, and z-planes of a point | Coordinates of points of interest on a 3D rendering, for export purposes |
| Mass [g] | The mass within contour(s) | Mass of cardiovascular structures of interest |
| Displacement [mm or degree] | The displacement vector represents the position of a point with respect to the position of that point in the reference (end diastole) phase. | Strain within cardiovascular structures of interest (e.g., myocardium) |
| Agatston Score [HU] | Industry-standard measure for coronary calcium based on volume and intensity of calcified plaque | For assessing overall calcified plaque burden in coronary arteries. |
| Angle [degrees] | The angle of an object/structure of interest | Angle between two lines of interest |
| Stenosis [%] | The narrowing of a vessel in area or diameter compared to a normal reference location | For measuring an abnormal narrowing in an artery |
| Velocity [mL/min or cm/s] | The velocity of moving objects within contour(s) | Velocity within cardiovascular structures of interest (e.g., blood flow) |
| Strain [%] | Strain is a measure of the deformation in shape and dimension of the heart muscle during the cardiac cycle. | Strain within cardiovascular structures of interest (e.g., myocardium) |

| | | |
|---|---|---|
| Strain Rate [1/s] | Derivative of strain with respect to time | Strain within cardiovascular structures of interest, as above |
| Time to Peak [ms] | Trigger time elapsed from the first phase till the phase where the peak strain has been reached. | Strain within cardiovascular structures of interest, as above |
| Torsion [degree/cm] | The difference in rotation between the apical and basal slices divided by the apical and basal slices. Note circumferential displacement represents an angle. | Strain within cardiovascular structures of interest, as above |
| End Diastolic Volume [mL] | LV/RV cavity volume at the phase defined as the ED | Calculated clinical data for LV/RV |
| End Systolic Volume [mL] | LV/RV cavity volume at the phase defined as the ES | Calculated clinical data for LV/RV |
| Stroke Volume [mL] | Stroke volume is the volume of blood pumped out of the LV/RV during each cardiac contraction and is represented by the difference of EDV and ESV. | Calculated clinical data for LV/RV |
| Ejection Fraction [%] | Ejection fraction is measured as a percentage of the total amount of blood in LV/RV that is pumped out with each cardiac cycle. It is calculated by dividing the SV by EDV. | Calculated clinical data for LV/RV |
| Cardiac Output [L/min] | Cardiac output is the amount of blood pumped by the heart in a minute and is calculated by multiplying the SV with heart rate per minute. | Calculated clinical data for LV/RV |
| Cardiac Index [L/min/$m^2$] | Cardiac index is a hemodynamic parameter that relates the CO from LV in one minute to BSA and is obtained by dividing the CO by BSA. | Calculated clinical data for LV |
| End Diastolic Mass [g] | LV myocardial mass at the phase defined as the ED and is calculated by multiplying the myocardial volume in ED phase with myocardial density (1.05 g/ml). | Calculated clinical data for LV |
| End Systolic Mass [g] | LV myocardial mass at the phase defined as the ES and is calculated by multiplying the myocardial volume in ES phase with myocardial density (1.05 g/ml). | Calculated clinical data for LV |
| Body Surface Area [$m^2$] | The total surface area of the body | Surface area of the patient body used in medical indicators or assessments |

## V. INTENDED USE / INDICATIONS FOR USE

Intended Use

cvi42 is intended to be used by qualified medical professionals for viewing, post-processing and quantitative evaluation of cardiovascular magnetic resonance (MR) images and cardiovascular computed tomography (CT) images in a Digital Imaging and Communications in Medicine Standard format, for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process

Indications for Use

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

It enables:

- Importing cardiac MR & CT Images in DICOM format.
- Supporting clinical diagnostics by qualitative analysis of cardiac MR & CT images using display functionality such as panning, windowing, zooming, navigation through series/slices and phases, 3D reconstruction of images including multiplanar reconstructions of the images.
- Supporting clinical diagnostics by quantitative measurement of the heart and adjacent vessels in cardiac MR & CT images, specifically signal intensity, distance, area, volume, and mass.
- Supporting clinical diagnostics by using area and volume for measuring cardiac function and derived parameters cardiac output and cardiac index in long axis and short axis cardiac MR & CT images.
- Flow quantifications based on velocity encoded cardiac MR images (including two and four dimensional flow analysis).
- Strain analysis of cardiac MR images by providing measurements of 2D LV myocardial function (displacement, velocity, strain, strain rate, time to peak, and torsion).
- Supporting clinical diagnostics of cardiac CT images including quantitative measurements of calcified plaques in the coronary arteries (calcium scoring), specifically Agatston and volume and mass calcium scores, visualization and quantitative measurement of heart structures including coronaries, femoral, aortic, and mitral valves.
- Evaluating CT and MR images of blood vessels. Combining digital image processing and visualization tools such as multiplanar reconstruction (MPR), thin/thick maximum intensity projection (MIP), inverted MIP thin/thick, volume rendering technique (VRT), curved planar reformation (CPR), 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 confirming the presence or absence of physician identified lesion in blood vessels and evaluation, documentation and follow up of any such lesions.

cvi42 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. cvi42 is a software application that can be used as a stand-alone product or in a networked environment.

The target population for cvi42 and its manual workflows is not restricted; however, cvi42's semi-automated machine learning algorithms, included in the MR Function and CORE CT modules, are intended for an adult population. Further, image acquisition by a cardiac MR or CT scanner may limit the use of the software for certain sectors of the general public.

cvi42 shall not be used to view or analyze images of any part of the body except the cardiac images acquired from a cardiovascular magnetic resonance or computed tomography scanner.

## VI. COMPARISON WITH PREDICATE DEVICE

The detailed analysis of the subject device and the predicate device (shown in **Table 2** and **Table 3**) demonstrates that the subject device is substantially equivalent in indications for use / intended use, technological characteristics, functionality, and operating principles with the predicates (K092628, K111373, K141480, K213998, K232661, and K241038). Of the three characteristics (technical, biological, and clinical) required for the demonstration of equivalence, biological characteristics are not applicable since both the subject device and predicate device are software as a medical device application with no tangible component interfacing with the body.

*Table 2. Subject Device Intended Use / Indications for Use*

| | **Subject Device**<br>*cvi42 Software Application (K242781)*<br>Manufactured by Circle |
|---|---|
| Intended Use | cvi42 is intended to be used by qualified medical professionals for viewing, post-processing and quantitative evaluation of cardiovascular magnetic resonance (MR) images and cardiovascular computed tomography (CT) images in a Digital Imaging and Communications in Medicine Standard format, for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process |
| Indications for Use | cvi42 is intended to be used for viewing, post-processing, qualitative and quantitative evaluation of cardiovascular magnetic resonance (MR) images and computed tomography (CT) images in a Digital Imaging and Communications in Medicine (DICOM) Standard format.<br><br>It enables:<br>• Importing cardiac MR & CT Images in DICOM format.<br>• Supporting clinical diagnostics by qualitative analysis of cardiac MR & CT images using display functionality such as panning, windowing, zooming, navigation through series/slices and phases, 3D reconstruction of images including multiplanar reconstructions of the images.<br>• Supporting clinical diagnostics by quantitative measurement of the heart and adjacent vessels in cardiac MR & CT images, specifically signal intensity, distance, area, volume, and mass.<br>• Supporting clinical diagnostics by using area and volume for measuring cardiac function and derived parameters cardiac output and cardiac index in long axis and short axis cardiac MR & CT images.<br>• Flow quantifications based on velocity encoded cardiac MR images (including two and four dimensional flow analysis).<br>• Strain analysis of cardiac MR images by providing measurements of 2D LV myocardial function (displacement, velocity, strain, strain rate, time to peak, and torsion).<br>• Supporting clinical diagnostics of cardiac CT images including quantitative measurements of calcified plaques in the coronary arteries (calcium scoring), specifically Agatston and volume and mass calcium scores, visualization and quantitative measurement of heart structures including coronaries, femoral, aortic, and mitral valves.<br>• Evaluating CT and MR images of blood vessels. Combining digital image processing and visualization tools such as multiplanar reconstruction (MPR), thin/thick maximum intensity projection (MIP), inverted MIP thin/thick, volume rendering technique (VRT), curved planar reformation (CPR), 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 confirming the presence or absence of physician identified lesion in blood vessels and evaluation, documentation and follow up of any such lesions.<br><br>cvi42 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. cvi42 is a software application that can be used as a stand-alone product or in a networked environment.<br><br>The target population for cvi42 and its manual workflows is not restricted; however, cvi42's semi-automated machine learning algorithms, included in the MR Function and CORE CT modules, are intended for an adult population. Further, image acquisition by a cardiac MR or CT scanner may limit the use of the software for certain sectors of the general public.<br><br>cvi42 shall not be used to view or analyze images of any part of the body except the cardiac images acquired from a cardiovascular magnetic resonance or computed tomography scanner. |

*Table 3. Predicate Device Intended Use / Indications for Use*

| | **Primary Predicate**<br>*cmr[42] (K082628)*<br>Manufactured by Circle | **Predicate**<br>*ct[42] (K111373)*<br>Manufactured by Circle | **Predicate**<br>*cvi42 (K141480)*<br>Manufactured by Circle | **Predicate**<br>*cvi42 Auto (K213998)*<br>Manufactured by Circle | **Predicate**<br>*Strain (K232661)*<br>Manufactured by Circle | **Predicate**<br>*CT Function (K241038)*<br>Manufactured by Circle |
|---|---|---|---|---|---|---|
| Intended Use | Viewing, post-processing, qualitative and quantitative evaluation of cardiovascular MR images in DICOM format. | Viewing, post-processing, qualitative and quantitative evaluation of cardiovascular CT 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 blood vessels and cardiovascular MR and CT images in DICOM format. | The Myocardial Strain Software Application is intended for qualitative and quantitative evaluation of cardiovascular MR images in a DICOM Standard format. As perquisite, the user confirms endocardial and epicardial contours in a reference phase, and the software tracks features over the cardiac cycle and computed 2D myocardial deformation and movement (e.g., strain, displacement, velocity). | The Cardiac CT Function Software Application is intended for qualitative and quantitative evaluation of cardiovascular CT images in a DICOM Standard format, to calculate and display cardiac function metrics (e.g., end diastolic volume, end systolic volume, stroke volume, ejection fraction, cardiac output, cardiac index, and LV myocardial mass). |
| Indications for Use | 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.<br><br>It enables;<br>• Importing Cardiac MR Images in DICOM format<br>• 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.<br>• Supporting clinical diagnostics by quantitative measurement of the heart and adjacent vessels in cardiac MR images, specifically distance, area, volume and mass<br>• 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.<br>• Flow quantifications based on velocity encodes 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.<br><br>It enables:<br>• Importing Cardiac CT Images in DICOM format<br>• 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.<br>• Supporting clinical diagnostics by quantitative measurement of the heart and adjacent vessels in cardiac CT images, specifically distance, area, volume and mass<br>• 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. | 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 multiplanar 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.<br><br>It shall be used by qualified medical professionals, experienced in examining and evaluating cardiovascular CT or MR images, for the purpose of obtaining diagnostic | 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.<br><br>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.<br><br>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.<br><br>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 | The Myocardial Strain Software Application is intended for qualitative and quantitative evaluation of cardiovascular magnetic resonance (CMR) images. It provides measurements of 2D LV myocardial function (displacement, velocity, strain, strain rate, time to peak, and torsion); these measurements are used by qualified medical professionals, experiences in examining and evaluating CMR images, for the purpose of obtaining diagnostic information for patients with suspected heart disease as part of a comprehensive diagnostic decision-making process. | The Cardiac CT Function Software Application is indicated to be use with multi-phase, multi-slice cardiovascular CT angiography images to assist qualified medical professionals in assessing and evaluating cardiac function. CT Function includes manual and semi-automatic heart segmentation of 2 chambers (LV and RV) and calculation of cardiac function metrics including end diastolic volume, end systolic volume, stroke volume, ejection fraction, cardiac output, cardiac index, and LV myocardial mass. |

| | **Primary Predicate**<br>*cmr$^{42}$ (K082628)*<br>Manufactured by Circle | **Predicate**<br>*ct$^{42}$ (K111373)*<br>Manufactured by Circle | **Predicate**<br>*cvi42 (K141480)*<br>Manufactured by Circle | **Predicate**<br>*cvi42 Auto (K213998)*<br>Manufactured by Circle | **Predicate**<br>*Strain (K232661)*<br>Manufactured by Circle | **Predicate**<br>*CT Function (K241038)*<br>Manufactured by Circle |
|---|---|---|---|---|---|---|
| | 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.<br><br>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.<br><br>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. | • Supporting clinical diagnostics by quantitative measurements of calcified plaques in the coronary arteries (calcium scoring), specifically Agatston and volume and mass calcium scores<br><br>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.<br><br>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.<br><br>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. | 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.<br><br>The target population for the cvi42 is not restricted. | images, for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process. | | |

*Table 3. Regulatory and technological features comparison.*

| **Feature** | **Subject Device**<br>*cvi42 Software Application (K242781)*<br>Manufactured by Circle | **Primary Predicate**<br>*cmr[42] (K082628)*<br>Manufactured by Circle | **Predicate**<br>*ct42 (K111373)*<br>Manufactured by Circle | **Predicate**<br>*cvi42 (K141480)*<br>Manufactured by Circle | **Predicate**<br>*cvi42 Auto (K213998)*<br>Manufactured by Circle | **Predicate**<br>*Strain (K232661)*<br>Manufactured by Circle | **Predicate**<br>*CT Function (K241038)*<br>Manufactured by Circle |
|---|---|---|---|---|---|---|---|
| Device Class | II | II | II | II | II | II | II |
| Device Classification | QIH, LLZ | LLZ | LLZ | LLZ | QIH, LLZ | LLZ | QIH, LLZ |
| Regulation Name | Medical image management and processing system | Picture Archiving and Communications System | Picture Archiving and Communications System | Picture Archiving and Communications System | Medical image management and processing system | Medical image management and processing system | Medical image management and processing system |
| Regulation Number | 21 CFR 892.2050 | 21 CFR 892.2050 | 21 CFR 892.2050 | 21 CFR 892.2050 | 21 CFR 892.2050 | 21 CFR 892.2050 | 21 CFR 892.2050 |
| Imaging Modalities | MR and CT | MR | CT | MR and CT | MR and CT | MR | CT |
| DICOM Compliant | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Import and display MR/CT images | Yes | Yes (MR only) | Yes (CT only) | Yes | Yes | Yes (MR only) | Yes (CT only) |
| Post process CMR/CCT images | Yes | Yes (MR only) | Yes (CT only) | Yes | Yes | Yes (MR only) | Yes (CT only) |
| Images can be displayed by study and series | Yes | Yes | N/A | N/A | N/A | N/A | N/A |
| Store images | Yes | Yes | N/A | N/A | N/A | N/A | N/A |
| 2D Imaging | Yes | Yes | N/A | N/A | N/A | N/A | N/A |
| 3D Imaging | Yes | No | Yes | Yes | Yes | Yes | Yes |
| Multiplanar Reformat (MPR) | Yes | No | Yes | Yes | Yes | No | Yes |
| Navigation Tools | Panning,<br>Windowing,<br>Zooming,<br>Series/slices and phases | Panning,<br>Windowing,<br>Zooming<br>Series/slices and phases | N/A | N/A | N/A | N/A | N/A |
| Measurements | Distance<br>Perimeter<br>Area<br>Signal Intensity<br>Volume<br>Coordinates<br>Mass<br>Displacement<br>Agatston Score<br>Angle<br>Stenosis<br>Velocity<br>Strain<br>Strain Rate<br>Time to Peak<br>Torsion<br>End Diastolic Volume (EDV)<br>End Systolic Volume (ESV)<br>Stroke Volume (SV)<br>Ejection Fraction (EF)<br>Cardiac Output (CO) | Distance<br>Perimeter<br>Area<br>Signal Intensity<br>Volume<br>Mass<br>Coordinates | Distance<br>Perimeter<br>Area<br>Signal Intensity<br>Volume<br>Coordinates<br>Agatston Score | Distance<br>Perimeter<br>Area<br>Signal Intensity<br>Volume<br>Coordinates<br>Angle<br>Stenosis | Distance<br>Perimeter<br>Area<br>Signal Intensity<br>Volume<br>Agatston Score<br>Stenosis<br>End Diastolic Volume (EDV)<br>End Systolic Volume (ESV)<br>Stroke Volume (SV)<br>Ejection Fraction (EF)<br>Cardiac Output (CO)<br>End Diastolic Mass (EDV)<br>End Systolic Mass (ESV)<br>Body Surface Area (BSA) | Displacement<br>Velocity<br>Strain<br>Strain Rate<br>Time to Peak<br>Torsion | End Diastolic Volume (EDV)<br>End Systolic Volume (ESV)<br>Stroke Volume (SV)<br>Ejection Fraction (EF)<br>Cardiac Output (CO)<br>Cardiac Index (CI)<br>End Diastolic Mass (EDM)<br>End Systolic Mass (ESM)<br>Body Surface Area (BSA) |

## cvi42 510(k) Summary

| **Feature** | **Subject Device**<br>*cvi42 Software Application (K242781)*<br>Manufactured by Circle | **Primary Predicate**<br>*cmr$^{42}$ (K082628)*<br>Manufactured by Circle | **Predicate**<br>*ct42 (K111373)*<br>Manufactured by Circle | **Predicate**<br>*cvi42 (K141480)*<br>Manufactured by Circle | **Predicate**<br>*cvi42 Auto (K213998)*<br>Manufactured by Circle | **Predicate**<br>*Strain (K232661)*<br>Manufactured by Circle | **Predicate**<br>*CT Function (K241038)*<br>Manufactured by Circle |
|---|---|---|---|---|---|---|---|
| | Cardiac Index (CI)<br>End Diastolic Mass (EDM)<br>End Systolic Mass (ESM)<br>Body Surface Area (BSA) | | | | | | |
| 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 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 using Machine Learning technique of four heart chambers in long and short-axis views | Manual segmentation, 2D functional analysis of myocardial deformation | Semi-automatic determination of epicardial and endocardial contours, via segmentation of the LV cavity, LV myocardium, and RV cavity and the ED and ES phases using Machine Learning Techniques |
| Assessment of cardiac blood flow | Quantification of blood flow using MR velocity encoded images. | Quantification of blood flow using MR velocity encoded images. | N/A | N/A | N/A | N/A | N/A |
| Centerline placement in coronary vessels | Manual and semi-automatic using Machine Learning technique | Manual | Manual and semi-automatic | Manual and semi-automatic | Manual and semi-automatic using Machine Learning technique | No | No |
| Calcium Scoring | Yes, using ML methodology | No | Yes, using non-ML methodology | No | Yes, using ML methodology | No | No |
| Workstation operating system | masOS,<br>Microsoft Windows | macOS,<br>Microsoft Windows | macOS,<br>Microsoft Windows | macOS,<br>Microsoft Windows | macOS,<br>Microsoft Windows | macOS,<br>Microsoft Windows | macOS,<br>Microsoft Windows |

**NOTE:** Some items have been marked Not Applicable (N/A), as this functionality is covered via other predicate devices in which the subject device is being compared to.

## VII. PERFORMANCE DATA AND TESTING

Performance testing was conducted to verify compliance with specified design requirements in accordance with ISO 13485:2016, BS EN 62304:2006, ISO 14971:2019, and DICOM standards.

Verification and validation testing were conducted to ensure specifications and performance of the device and were performed per the FDA Guidance *"Technical Performance Assessment of Quantitative Imaging in Radiological Device Premarket Submission"*. No clinical studies were necessary to support substantial equivalence.

cvi42 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.'s software development as described in the company's product development process.

**Validation of non-Machine Learning Outputs**

The validation of non-ML or rule-based algorithms and mathematical outputs in cvi42 is performed through general in-house software QA verification and validation process including unit tests, content/phantom tests, quantitative and qualitative analysis, and visual/manual evaluation. Some more complex algorithms, such as Strain measurement, however, have undergone additional validation to ensure the safe and effective use of the software.

Strain: 2D LV

The tracking performance and the clinically relevant Global Longitudinal and Global Circumferential strains were validated using a complimentary combination of simple and realistic phantoms, real MRI data, and analytical solutions. The tracking performance was evaluated with simple analytical phantoms generated with variable input parameters; the deformation field generated by the strain module was evaluated on realistic phantoms with artificially imposed known deformation field and perturbations; and the performance of the constrained tissue tracking algorithm was also compared to manual tracking in ES phase by three expert readers. The computation of the deformation metrics from the tracked deformations were evaluated analytically.

## Validation of Machine Learning Derived Outputs

The machine learning algorithms of cvi42 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. In general, image information for samples is anonymized and limited to ePHI-free DICOM headers and at least 50% of the data came from a U.S. population. All performance testing results have met Circle's pre-defined acceptance criteria.

cvi42 Auto: MR Function & CORE CT

The machine learning algorithms of cvi42 Auto (MR-CMR Function, CORE CT Coronary, and CORE 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%.

CORE CT: CT Function

The Machine Learning (ML) algorithms of the CT Function Module have been trained and tested on images acquired from major vendors of CT imaging devices. All data used for validation were not used during the development of the ML algorithms. Image information for all samples was anonymized and limited to ePHI-free DICOM headers. The validation data was sourced from 9 different sites, with 90% of the data sampled from US sources. All performance testing results met Circle's pre-defined acceptance criteria.

For cardiac CT function analysis, the acceptance criteria were pre-defined to evaluate the

performance of the ML-based segmentation of Left Ventricle (LV) cavity, LV myocardium, and Right Ventricle (RV) cavity. The mean volume prediction error (Mean Absolute Error in predicted volumetric measures, or MAE), 3D Hausdorff Distance (HD), and Dice coefficient were used to evaluate the performance of the segmentation. Overall, comparable performance was achieved on all variability factors including scanner vendors, scanner tube current, pixel resolution, slice thickness, age group, and gender.

Compared to a reference standard established from three expert readers, the ML-based model is capable of segmenting the LV cavity with less than 10% difference in MAE, a Dice coefficient above 86%, a HD below 9.5 mm, and an EF bias of 1.3% with a 95% confidence interval of [-12, 14]. Similarly, the RV cavity is segmented with less than 18% MAE, a Dice coefficient above 85%, a HD below 18 mm, and an EF bias of -5.5% with a 95% confidence interval of [-15, 4.4]. Lastly, the LV myocardium is segmented with less than 17% MAE, a Dice coefficient above 82%, and a HD below 15 mm.

## VIII. CONCLUSION

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