



February 20, 2025

Caristo Diagnostics Ltd.
% John Smith
Partner
Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
WASHINGTON DC 20004

Re: K242240

Trade/Device Name: CaRi-Plaque
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management And Processing System
Regulatory Class: Class II
Product Code: LLZ
Dated: July 30, 2024
Received: January 16, 2025

Dear John Smith:

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,



, for

Jessica Lamb
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

Indications for Use

510(k) Number (if known)
K242240

Device Name
CaRi-Plaque

Indications for Use (Describe)

CaRi-Plaque is intended to provide an optimized non-invasive application to analyze coronary anatomy and pathology and aid in determining treatment paths from a set of Computed Tomography (CT) Angiographic images.

CaRi-Plaque is a web-based image processing application. It is a non-invasive diagnostic reading software intended for use as an interactive tool for viewing and analyzing cardiac CT data for determining the presence and extent of coronary plaques and luminal stenoses.

CaRi-Plaque is intended for use by internal operators who have been appropriately trained in the software's functions, capabilities and limitations.

Users should be aware that certain views make use of interpolated data. This is data that is created by the software based on the original data set. Interpolated data may give the appearance of healthy tissue in situations where pathology may be present that is near or smaller than the scanning resolution.

The analysis results produced by the software and provided to the Healthcare Professional are not intended to replace the skill and judgment of a qualified medical practitioner. The analysis results should be reviewed with other clinical information which may include but is not limited to: The patient's original CT images, clinical history, symptoms, clinical risk factors, results of other diagnostic tests, and the clinical judgement of appropriately qualified Healthcare Professionals.

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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510(k) SUMMARY
Caristo's CaRi-Plaque

Submitter and 510(k) Owner

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Official Correspondent

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Date of Preparation: February 11, 2025
Name of Device: CaRi-Plaque
Classification Name: Radiological Image Processing System
Regulatory Class: Class II
Product Code: LLZ
Regulation: 21 CFR §892.2050
Predicate Device: Autoplaque 3.0 (K212758, Cedars-Sinai Medical Center)
Reference Device: CaRiCloud v1.0 (K200274, Caristo Diagnostics)

Device Description

CaRi-Plaque v1.0 ("CaRi-Plaque," the subject device) is a web-based software-only application for the quantitative and qualitative clinical analysis of previously acquired CCTA DICOM data for the purpose of characterizing and quantifying plaque formation and stenosis in coronary arteries. CaRi-Plaque aids healthcare professionals trained in cardiovascular health and patient care (including but not limited to Cardiologists, Radiologists and others) by describing the physical characteristics of coronary plaque volume and cross-sectional area, determined using a combination of 3D image thresholding computerized algorithms and manual editing tools to provide automated quantification and characterization of coronary atherosclerotic plaque and stenosis. The processing of CT scan data is performed by trained operators and the resulting CaRi-Plaque Report is provided to the healthcare professional to enable them to assess the extent and severity of coronary disease.

The CaRi-Plaque report includes visual representations of each vessel and associated quantitative outputs. These quantitative outputs include: Plaque Burden, Calcified Plaque (CP) Volume, Total Plaque

Volume, Noncalcified Plaque (NCP) Volume, Low Density Noncalcified Plaque (LD-NCP) Volume, Remodeling Index, and Maximum Stenosis. CaRi-Plaque does not replace standard clinical practice or clinical decision-making, and the results of the CaRi-Plaque analysis are to be used in the context of other patient information by the healthcare professional. The healthcare professional may request a re-analysis of the CT scan data if they do not agree with the report analysis.

Intended Use / Indications for Use

CaRi-Plaque is intended to provide an optimized non-invasive application to analyze coronary anatomy and pathology and aid in determining treatment paths from a set of Computed Tomography (CT) Angiographic images.

CaRi-Plaque is a web-based image processing application. It is a non-invasive diagnostic reading software intended for use as an interactive tool for viewing and analyzing cardiac CT data for determining the presence and extent of coronary plaques and luminal stenoses.

CaRi-Plaque is intended for use by internal operators who have been appropriately trained in the software's functions, capabilities and limitations.

Users should be aware that certain views make use of interpolated data. This is data that is created by the software based on the original data set. Interpolated data may give the appearance of healthy tissue in situations where pathology may be present that is near or smaller than the scanning resolution.

The analysis results produced by the software and provided to the Healthcare Professional are not intended to replace the skill and judgment of a qualified medical practitioner. The analysis results should be reviewed with other clinical information which may include but is not limited to: The patient's original CT images, clinical history, symptoms, clinical risk factors, results of other diagnostic tests, and the clinical judgement of appropriately qualified Healthcare Professionals.

Comparison to the Predicate Device

The overall intended use for CaRi-Plaque is the same as the predicate device: both devices are intended to process radiological images and provide measurements of anatomical components in those images. Furthermore, the subject device's indications for use statement is similar to the predicate device. Both devices are indicated to provide an optimized non-invasive application to analyze coronary anatomy and pathology from CT angiographic images, to provide a post-processing tool for viewing and analyzing cardiac CT data for determining the presence and extent of coronary plaques and luminal stenosis, and to provide analysis results to aid in the determination of treatment paths by the healthcare professional, in conjunction with other patient data. Additionally, both devices are indicated for use by trained operators.

The differences in indications for use between the subject device and predicate device do not cause the subject device to have a different overall intended use. In particular, the location of use for the software operator differs, as CaRi-Plaque is indicated as a web-based application that can be operated off-site with imaging data transmitted via web-based software, while the predicate device is indicated as a workstation-based desktop device for use at clinical sites. However, for both devices the final analysis results are indicated to be provided to a healthcare professional for use at a clinical location. Therefore, the indicated recipients and locations of application of the final device output are the same for both devices. Of note, the location of use and workflow of the CaRi-Plaque software is the same as the

CaRiCloud reference device – i.e., trained operators located in regional data centers use the software device to perform an analysis and generate a report that is subsequently provided to a healthcare professional end user.

Comparison of Technological Characteristics

The technology of CaRi-Plaque is similar to the predicate device (see Table 1). Both devices analyze CT angiographic images for the presence and extent of coronary plaque and luminal stenosis. In addition, they both require trained operators to perform the assessment. Both devices provide equivalent quantitative measurements in a report to the healthcare professional after completing the analysis. These reports are intended to be reviewed by the healthcare professional and used in conjunction with other patient information, such as the original CT images, clinical history, symptoms, clinical risk factors, results of other diagnostic tests, and the clinical judgement of the ordering prescriber. Both devices have demonstrated agreement between clinical expert readers and software measurements in clinical performance testing and have demonstrated appropriate inter-operator and intra-operator agreement.

There are three key technological differences between the subject device and the predicate. First, the location of the DICOM image data is different: The CaRi-Plaque Cloud software is web-based and receives DICOM images via transmittal by a secure picture archiving and communication system (PACS), while the AutoPlaque predicate software resides on a commercial computer platform at the clinical site and receives DICOM image data via loading from the local computer hard drive. Second, the location of the trained software operator may be different: The subject device operator can be at a remote site, while the predicate device operator is at the clinical site on a desktop computer. For both devices, the software operators are trained to review anatomy, define and correct the vessels of interest and generate a report. In both cases, the healthcare professional end user can repeat (or request the repeat of) the analysis if needed. The third difference is that the methods of developing segmentation and plaque calculation algorithms differ for the subject versus the predicate device, as the subject device uses threshold-based segmentation while the predicate device uses machine learning to train the algorithms. This technological methodology difference does not raise questions of differences in safety or effectiveness because the algorithms of both devices are intended to accomplish the same indicated uses and were verified and validated using the same clinical testing approach in which device outputs are compared to expert-determined ground truth. Furthermore, as discussed below in the Performance Testing section, the CaRi-Plaque software met all acceptance criteria in the clinical validation study, showing an excellent correlation between CaRi-Plaque measurements and ground truth by expert readers for the same endpoints that the predicate device used in its clinical performance testing.

Therefore, the minor technological differences between the subject and predicate device do not raise different questions of safety or effectiveness.

Table 1. Technology Comparison to Predicate

Parameter	CaRi-Plaque Subject Device	Autoplaque 3.0 (K212758) Predicate Device
Computer Operating System	Client-side Google Chrome application	Windows / Mac OS
Stand-alone software	Yes	Same
DICOM Compliance	DICOM 3	Same
2D Imaging	Review of coronary vessels in 2D MPR, curved MPR, and straightened view.	Same
2D Measurement	2D measurement tools of vessel diameter and contour	Same
3D Imaging	Review of structures in 3D	Same
Maximum intensity projection (MIP)	N/A; this visualization method is not necessary analyzing the presence and extent of coronary plaque and luminal stenosis	MIP with interactive control
Multiplanar reformatting (MPR)	MPR with oblique slicing. Variable slab thickness is not necessary analyzing the presence and extent of coronary plaque and luminal stenosis	MPR with oblique slicing and variable slab thickness
Quantitative Measurements		
Diameter stenosis: Maximum diameter stenosis, with respect to proximal and distal references	Yes	Same
Total Plaque Volume	Yes	Same
Calcified Plaque Volume	Yes	Same
NCP volume: noncalcified plaque volume	Yes	Same
LD-NCP volume: low-density noncalcified plaque volume	Yes	Same
Vessel Volume	No. This is calculated but not reported as a device output.	Yes
NCP burden: noncalcified plaque volume / analyzed vessel volume	No	Yes
LD-NCP burden: low-density noncalcified plaque volume / analyzed vessel volume	No	Yes
CP burden: calcified plaque volume/analyzed vessel volume	No	Yes
Total plaque burden: total plaque volume/analyzed vessel volume	Yes	Same
Plaque composition NCP: noncalcified plaque composition (NCP volume / total plaque volume)	No	Yes
Plaque composition CP: calcified plaque composition (CP volume / total plaque volume)	No	Yes
Plaque composition LDNCP: low-density noncalcified plaque	No	Yes

Parameter	CaRi-Plaque Subject Device	Autoplaque 3.0 (K212758) Predicate Device
composition (LD-NCP volume / NCP volume)		
QCAD: Maximum diameter stenosis	Yes, refers to a single reference site	Yes, refers to proximal and distal references
Remodeling index: ratio of maximum vessel area / proximal and distal references	Yes	Same
Area stenosis: maximum area stenosis, with respect to proximal and distal references	Yes	Same
Plaque length: diseased vessel length	No. This is calculated but not reported as a device output.	Yes
Contrast density difference: maximum difference in contrast density over lesion with respect to proximal	No; not used as a common reference standard	Yes
MLD: minimal luminal diameter over lesion	No. This is calculated but not reported as a device output.	Yes
MLA: minimum luminal area over lesion	No	Yes
Vessel profile: area, maximum diameter, minimum diameter measured from selected vessel cross section	Yes	Same
Lumen profile: area, maximum diameter, minimum diameter measured from selected lumen cross section	Yes	Same
Vessel, plaque, and lumen segmentation	Yes- semi-automatic (threshold-based segmentation with full option to edit); output demonstrated to meet pre-determined acceptance criteria in clinical performance study	Yes- semi-automatic (deep learning based with full option to edit)

Performance Testing

The 510(k) submission provided performance data to establish the substantial equivalence of CaRi-Plaque (the subject device) to the predicate device. A summary of these performance tests is provided below.

Software Verification and Validation:

Software verification and validation testing were conducted to demonstrate that the subject device meets specifications and works as intended.

Clinical Validation Study:

A clinical performance test was conducted to compare plaque characteristics reported with CaRi-Plaque to ground truth determined by qualified independent medical experts. The study determined the degree of consistency between plaque characteristics reported by CaRi-Plaque and independent medical expert readers using a multi-center, international patient population in 117 subjects (85 men, 32 women) aged 27 to 85 years of age from four (4) sites (2 US and 2 OUS). Individual subject-level ethnicity was collected at two of the four study sites. This gave the following breakdown for 57 subjects: White 76%, Asian 4%,

Middle Eastern 1%, other 14%, and unknown 5%. For the two remaining sites, ethnicity was estimated from local population census data (www.census.gov). This gave the following breakdown for the first site (48 subjects): White (not Hispanic or Latino) 44%, Black 22%, Hispanic or Latino 27%, and Asian 5%; and for the second site (12 subjects): White (not Hispanic or Latino) 46%, Black 19%, Hispanic or Latino 26%, and Asian 13%. The CT scanners to collect images included commercial CT scanners from Toshiba, GE, Phillips, and Siemens. Qualified independent medical experts performed ground truthing.

The study established agreement between the expert readers and the CaRi-Plaque device measurements for Maximum Stenosis, Total Plaque Volume, Calcified Plaque Volume and Noncalcified Plaque Volume using the acceptance criteria of Pearson Correlation Coefficients for each metric. Agreement was also reported for Plaque Burden, Low Density Noncalcified Plaque Volume and Remodeling Index. The Pearson Correlation Coefficients for Maximum Stenosis, Total Plaque Volume, Calcified Plaque Volume, Noncalcified Plaque Volume, Plaque Burden and Low Density Noncalcified Plaque Volume were 0.930, 0.985, 0.999, 0.977, 0.885, 0.817, respectively. These results met the predetermined acceptance criteria. Remodeling Index was assessed using Cohen's Kappa with an agreement of 63.3% ($K = 0.42$). Subgroup analysis by vessel, sex and age did not reveal any bias in performance.

Agreement between the expert readers and the CaRi-Plaque device measurements at the branch level were reported using Pearson Correlation Coefficients (or Cohen's Kappa for remodeling index). For RCA, R-PDA and R-PLB: Maximum Stenosis, Total Plaque Volume, Calcified Plaque Volume, Noncalcified Plaque Volume, Plaque Burden, Low Density Noncalcified Plaque Volume and Remodeling Index were 0.863, 0.958, 0.964, 0.953, 0.924, 0.633, 90.3% ($K=0.31$), respectively. For LAD, D1, D2 and Ramus: Maximum Stenosis, Total Plaque Volume, Calcified Plaque Volume, Noncalcified Plaque Volume, Plaque Burden, Low Density Noncalcified Plaque Volume and Remodeling Index were 0.929, 0.959, 0.997, 0.942, 0.913, 0.802, 87.2% ($K=0.44$), respectively. For LCX, OM1 and OM2: Maximum Stenosis, Total Plaque Volume, Calcified Plaque Volume, Noncalcified Plaque Volume, Plaque Burden and Remodeling Index were 0.911, 0.948, 0.991, 0.934, 0.888, 0.633, 90.3% ($K=0.31$), respectively. There was insufficient low density non-calcified plaque in the LCX, OM1 and OM2 to generate a meaningful correlation.

Additionally, there was good inter-operator agreement and repeatability at the branch level within the CaRi-Plaque device arm and between readers in the Ground Truth arm.

Conclusion

The information provided above supports that CaRi-Plaque is as safe and effective as the predicate device. The device has the same intended use as the predicate device, and minor differences in indications for use do not alter the intended use of the device and do not affect its safety and effectiveness. In addition, the minor technological differences between the devices do not raise different questions of safety or effectiveness, and they are addressed through software verification and validation testing and a clinical validation study. Therefore, CaRi-Plaque is substantially equivalent to the predicate device.