Siemens Healthcare GmbH
℅ Mr. Abhineet Johri
Regulatory Affairs Manager
Siemens Medical Solutions, Inc.
65 Valley Stream Parkway
MALVERN PA 19355

March 9, 2020

Re: K193216
Trade/Device Name: syngo.CT Lung CAD
Regulation Number: 21 CFR 892.2050
Regulation Name: Picture archiving and communications system
Regulatory Class: Class II
Product Code: OEB
Dated: February 4, 2020
Received: February 6, 2020

Dear Mr. Johri:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for

devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

K193216

Device Name

syngo.CT Lung CAD (VC30)

Indications for Use *(Describe)*

The syngo.CT Lung CAD VC30 device is a Computer-Aided Detection (CAD) tool designed to assist radiologists in the detection of solid pulmonary nodules during review of multi-detector computed tomography (MDCT) examinations of the chest. The software is an adjunctive tool to alert the radiologist to regions of interest that may have been initially overlooked. The syngo.CT Lung CAD device is intended to be used as a second reader after the radiologist has completed his/her initial read.

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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K193216

510(k) Summary

for

Siemens Healthcare GmbH

syngo.CT Lung CAD

(Previously cleared as *syngo.CT* Lung CAD, K143196)

Version VC30

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR §807.92.

Date prepared: March 05, 2020

1. **Submitter (Legal Manufacturer):**
   Siemens Healthcare GmbH
   Henkestrasse 127
   91052 Erlangen
   Germany

   Manufacturing Location (Facility)

   Siemens Medical Solutions USA, Inc.
   65-3 Valley Stream Parkway
   Malvern PA. 19355

   Establishment Registration Number:
   3004977335

2. **Contact Person:**
   Mr. Abhineet Johri
   Regulatory Affairs Manager
   Siemens Healthcare GmbH,
   65-3 Valley stream parkway
   Malvern, PA 19355.
   U.S.A
   E-mail: abhineet.johri@siemens-healthineers.com
   Telephone: +1 (484) 680-8723
   Fax: +1 610-448-6557

3. **Device Name and Classification:**

Trade Name:	*syngo*.CT Lung CAD
Classification Name:	Lung computed tomography system, computer-aided detection
Classification Panel:	Radiology
CFR Section:	21 CFR §892.2050
Device Class:	Class II
Product Code:	OEB

4. Legally Marketed Predicate Device:

Trade Name:	*syngo*.CT Lung CAD
510(k) Clearance:	K143196
Clearance Date:	May 2015
Classification Name:	Lung computed tomography system, computer-aided detection
Classification Panel:	Radiology
CFR Section:	21 CFR §892.2050
Device Class:	Class II
Product Code:	OEB
Recall Information:	This predicate device has not been the subject of any design related recalls.

5. Device Description:

Siemens Healthcare GmbH intends to market the *syngo*.CT Lung CAD which is a medical device that is designed to perform CAD processing in thoracic CT examinations for the detection of solid pulmonary nodules ≥ 3.0 mm in size. The device processes images acquired with Siemens multi-detector CT scanners with 4 or more detector rows.

The *syngo*.CT Lung CAD device supports the full range of nodule locations (central, peripheral) and contours (round, irregular). The detection performance of the *syngo*.CT Lung CAD device is optimized for nodules between 3.0 mm and 20.0 mm in size.

The *syngo*.CT Lung CAD sends a list of nodule candidate locations to a visualization application, such as *syngo* MM Oncology, or a visualization rendering component, which generates output images series with the CAD marks superimposed on the input thoracic CT images for use in a second reader mode. *syngo* MM Oncology (FDA clearance k191309) is implemented on the *syngo*.via platform (FDA clearance k191040), which provides a common framework for various other applications implementing specific clinical workflows (but are not part of this clearance) to display the CAD marks. The *syngo*.CT Lung CAD device is intended to be used as a second reader only after the initial read is completed.

The subject device and the predicate device has the same basic technical characteristics as the predicate; however, the fundamental technology has been replaced by deep learning technology. Specifically, the predicate VC20 uses feature-based and Machine Learning whereas the current VC30 uses algorithms based on Convolutional Neural Networks. This does not introduce new types of safety or effectiveness concerns. In particular, as demonstrated by the statistical analysis and results of the standalone benchmark evaluations:

i. The standalone accuracy has been shown not only to be non-inferior but actually superior to that of the device and
ii. The marks generated by the two devices have been shown to be reasonably consistent.

This device description holds true for the subject device, *syngo*.CT Lung CAD, software version VC30, as well as the predicate device, *syngo*.CT Lung CAD, software version VC20.

6. Intended Use:

The *syngo*.CT Lung CAD device is a computer-aided detection (CAD) tool designed to assist radiologists in the detection of solid pulmonary nodules during review of multi-detector computed tomography (MDCT) examinations of the chest. The software is an adjunctive tool to alert the radiologist to regions of interest (ROI) that may have been initially overlooked. The *syngo*.CT Lung CAD device is intended to be used as a second reader after the radiologist has completed his/her initial read.

Safety and Effectiveness Information

Software design description, hazard analysis, and technical and safety information have also been completed and provided in support of this device. The results of the hazard analysis, combined with the appropriate preventive measures taken indicate the device is of moderate level of concern, as per Guidance for the Content of Premarket Submission for Software Contained in Medical Devices, May 2005

The device has no patient contacting materials and is utilized only by trained professionals. The output of the device is evaluated by trained professionals as a second reader. Use of this device does not impact the quality or status of the original acquired data.

Substantial Equivalence:

The *syngo*.CT Lung CAD is substantially equivalent, both in intended use and indication for use to the following device. The new version has the same basic technical characteristics as the predicate; however, the fundamental technology has been replaced by deep learning technology. Specifically, the predicate VC20 uses feature-based ML CADe compared to current VC30 deep CNN-based CADe. This does not introduce new types of safety or effectiveness questions. As demonstrated by the statistical analysis and results of the standalone benchmark evaluations:

iii. The standalone accuracy has been shown not only to be non-inferior but actually superior to that of the device and

iv. The marks generated by the two devices have been shown to be reasonably consistent.

Company	Product – Trade Name	510(k) #
Siemens AG Medical Solutions	*Syngo*.CT Lung CAD	K143196

In summary, Siemens Healthcare GmbH is of the opinion that the *syngo*.CT Lung CAD software, as described within this document, does not pose any unmitigated safety risks and is substantially equivalent to the predicate device since its accuracy has been shown to be superior to the predicate device and the marks are reasonably consistent .

The difference between the predicate device *syngo*.CT Lung CAD VC20 and *syngo*.CT Lung CAD VC30 are minor in nature and both devices have the same characteristics and functionalities, as described in table below.

7. Summary of Differences between the Subject Device and the Predicate Device:

The differences between the subject device described in this premarket notification and the predicate device are summarized in the following comparison table 1 and 2 below:

Subject Device Characteristic	**Current Predicate Device *syngo*.CT Lung CAD (VC20E) (K)143196**	**New Device *syngo*.CT Lung CAD (VC30)**	**Type of Change and Impact to Safety & Effectiveness**
Manufacturer	Siemens AG Medical Solutions	Siemens Healthcare GmbH	Legal manufacturer change[1]. No Impact
Detection target	Solid pulmonary nodules in diagnostic chest CT acquisitions	Solid pulmonary nodules in diagnostic chest CT acquisitions	[Unchanged] and no Impact
Intended Use	The LungCAD software device is a Computer-Aided Detection (CAD) tool designed to assist radiologists in the detection of solid pulmonary nodules during review of multi-detector computed tomographic (MDCT) thoracic examinations. The software is an adjunctive tool that alerts the radiologist to regions of interest (ROI) that may be initially overlooked. The LungCAD software device use is intended to be used as a second reader after the radiologist has completed his/her initial read.	The LungCAD software device is a Computer-Aided Detection (CAD) tool designed to assist radiologists in the detection of solid pulmonary nodules during review of multi-detector computed tomographic (MDCT) thoracic examinations. The software is an adjunctive tool that alerts the radiologist to regions of interest (ROI) that may be initially overlooked. The LungCAD software device use is intended to be used as a second reader after the radiologist has completed his/her initial read.	[Unchanged] and no Impact

[1] syngo.CT Lung CAD (VC20)was manufactured by Siemens AG Medical Solutions during the time of its filing. Later-on legal manufacturer change was performed to Siemens Healthcare GmbH. So finally, the legal manufacturer is identical for both devices.

Indications For Use	• The *syngo*.CT Lung CAD device is a computer-aided detection (CAD) tool designed to assist radiologists in the detection of solid pulmonary nodules during review of multi-detector computed tomography (MDCT) examinations of the chest. • The software is an adjunctive tool to alert the radiologist to regions of interest (ROI) that may have been initially overlooked. • The *syngo*.CT Lung CAD device is intended to be used as a second reader after the radiologist has completed his/her initial read.	• The *syngo*.CT Lung CAD device is a computer-aided detection (CAD) tool designed to assist radiologists in the detection of solid pulmonary nodules during review of multi-detector computed tomography (MDCT) examinations of the chest. • The software is an adjunctive tool to alert the radiologist to regions of interest (ROI) that may have been initially overlooked. • The *syngo*.CT Lung CAD device is intended to be used as a second reader after the radiologist has completed his/her initial read.	[Unchanged] and no Impact
Nodule Characteristics	Size • Solid nodules ≥ 3mm and ≤ 10mm Locations • full range: central, peripheral Contours: • round, irregular	Diameter • Solid nodules ≥ 3mm and ≤ 20mm Locations • full range: central, peripheral Contours: • round, irregular	Extended nodule size to 20mm. No impact as assessed in the evidence provided in the benchmark analysis provided in this substantial equivalence evaluation. Attachment 10 and 12

Reader workflow	second reader workflow	second reader workflow	[Unchanged] and no Impact
Input scanning parameters	**Scanners** Siemens multi-detector CT (MDCT) scanners.	**Scanners** Siemens multi-detector CT (MDCT) scanners.	[Unchanged] and no Impact
	Detector rows 4 or more detector rows	**Detector rows** 4 or more detector rows	[Unchanged] and no Impact
	Scan area The scan area needs to comprise the entire thorax covering the lung apices to the bases	**Scan area** The scan area needs to comprise the entire thorax covering the lung apices to the bases	[Unchanged] and no Impact
	Scan direction Cranio-caudal or caudal-cranial	**Scan direction** Cranio-caudal or caudal-cranial	[Unchanged] and no Impact
	Voltage 120 -140 kVp	**Voltage** 120 -140 kVp	[Unchanged] and no Impact
	Exposure 40–120 mAs	**Exposure** 40–120 mAs	[Unchanged] and no Impact
	Collimation 1 mm or less	**Collimation** 1 mm or less	[Unchanged] and no Impact
	Slice width 1.00 - 1.25 mm	**Slice Thickness** 1.00 - 1.25 mm	[Unchanged] and no Impact – nomenclature updating only
	Slice overlap 0–25% Note: Reconstruction overlap is allowed, but gaps are not permitted	**Slice Overlap** 0–25% Note: Reconstruction overlap is allowed, but gaps are not permitted	[Unchanged] and no Impact
	Number of images Up to 1000 images per series.	**Number of images** Up to 1000 images per series.	[Unchanged] and no Impact

	Kernel Siemens B60	**Kernel** Siemens B60	[Unchanged] and no Impact
Hosting Platform	*syngo*.via	*syngo*.via	[Unchanged] and no Impact
Hosting Application	*syngo* MM Oncology	*syngo* MM Oncology	[Unchanged] and no Impact
Dose	Diagnostic	Diagnostic	[Unchanged] and no Impact

Table 1 Summary of Differences between the Subject Device and the Predicate Device

Functional Component	**LungCAD VC20**	**LungCAD VC30**
Preprocessing Standardization of the input images and lung segmentation	(a) isotropic volume resampling (b) lung segmentation is performed on a slice-by-slice approach by identifying the middle of the lung area, then processing first the upper half of the lung and then the lower half of the lungs. Slice processing identifies starting points and traces the lung contour, slice-by slice. This is followed by contour smooth and filling.	(a) isotropic volume resampling (b) lung segmentation is accomplished using a CCN. Initially a coarse estimation of the lung is performed using a V-net process. Using two predefined bounding boxes left and right lungs are initialized. Another V-net is used to segment left and right lungs. This is followed by up-sampling to the original image resolution.
Candidate Generation Scans through all slices of the segmented lung to search for	(a) isotropic volume is partitioned into subvolumes (b) Each volume is processed using the divergence of the 3D gradient field compute a "response volume" thresholded to yield a list of candidates. Features are computed (e.g. number of voxels, sphericity, maximum response value, etc.) (c) Cascade 1: candidates are passed to two-way	(a) isotropic volume is partitioned into subvolumes (b) Each subvolume is fed to a CNN to compute features ("response volume"). Filtering and non-maximum suppression yield a list of candidates for each subvolume (c) Cascade 1: candidates above a certain threshold score are passed to the next step.

candidates	gaiting classifier. Those above a certain threshold score are kept and passed to the next step.	
Feature Calculation Features are computed for each candidate.	Groups of features are computed for each candidate. These groups of features include: Gaussian, curvature , isotropy, wall attachment, etc.	CNN is used for feature computation for each candidate. (a) The input image patch is firstly processed by batch normalization. (b) Three blocks of operations are computed. In each block, a convolution, with stride 2, is used for down-sampling instead of max-pooling. (c) Semantic features from image features are computed using two fully connected layers.
Candidate Classification Candidate specificity is increased by applying a logistic regression classifier to the hierarchical features calculated	Cascade 2: (a) A three way-gaiting classifier is applied to each candidate based on values computed in the previous section. (b) Based on the gaiting, the features from previous step are used to assign a label to the candidate .	CNN is used for candidate classification . (a) A soft-max function, applied to each candidate, assigns 2 values corresponding to the probability of being a nodule or being a false positive. (b) Cascade 2: A weighted-sum of the scores from Cascade 1 and the results of the classifier (prior step) is computed. Candidates above a certain threshold score are labeled as nodule candidates.
Final Candidate List	The location information of the nodule candidates are collected into a final candidate list passed to the hosting application	The location information of the nodule candidates are collected into a final candidate list passed to hosting application.

Table 2: Functional Components for syngo.CT Lung CAD VC20 (predicate) and syngo.CT Lung CAD VC30 (Subject device)

8. Non-clinical Performance Testing:

Non-clinical tests were conducted for the device *syngo*.CT Lung CAD (during product development. The modifications described in this Premarket Notification were supported with verification and validation testing.

Siemens Healthcare GmbH claims conformance to the following standards:

- ISO 14971 Second edition 2007-03-01
- IEC 62304 Edition 1.1 2015-06 Consolidated Version
- IEC 62366-1 Edition 1.0 2015-02

9. Software Verification and Validation:

Software documentation for a Moderate Level of Concern software per FDA's Guidance Document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" issued on May 11, 2005 is also included as part of this submission. The performance data demonstrates continued conformance with special controls for medical devices containing software. Non-clinical tests were conducted on the device *syngo*.CT Lung CAD during product development.

The Risk Analysis was completed, and risk control implemented to mitigate identified hazards. The testing results support that all the software specifications have met the acceptance criteria. Testing for verification and validation for the device was found acceptable to support the claims of substantial equivalence.

Summary:
Performance tests were conducted to test the functionality of the device *syngo*.CT Lung CAD . These tests have been performed to assess the functionality of the subject device. Results of all conducted testing were found acceptable in supporting the claim of substantial equivalence.

The standalone performance test proved that the standalone sensitivity of *syngo*.CT Lung CAD VC30 is superior to that of *syngo*.CT Lung CAD VC20 (predicate) and the false positive rate improved (reduced). Furthermore, both true positive and false positive *syngo*.CT Lung CAD VC30 marks were shown to be reasonably consistent with marks produced by *syngo*.CT Lung CAD VC20 (predicate) in both location and extent. The endpoints to establish meaningful and statistically relevant performance and equivalence of the device and sample size were considered and defined as part of the test protocols.

Non-clinical performance testing was performed at various levels for verification and validation of the device intended use and to ensure safety and effectiveness.

The protocol of the tests follows the testing activities of the software development and quality management process. This protocol, which ensures both verification and validation, is structured at different levels of product testing to ensure that the above objectives are met. These are:

1. Unit test: Verify the Design Specification, Risk Mitigations, identify runtime errors and memory leaks and Verify the Logic.
2. Integration test: Verify the correct implementation of the design and test coverage specified by the software requirements and Design Specifications. The Implementation and effectiveness of Risk mitigation classified as Hazard is also checked. (Hazard Tests).
3. System test: It is performed on the integrated product comprising of the software units and components.
4. System Validation: Objective is to validate the intended use defined in the requirements specifications and risk labelling mitigations. These requirements will be validated using one of the Hosting Applications.

Tests specifications used for the test levels mentioned above include test descriptions, test environment and the test cases with the requirements that were tested. Tests are passed only based on the defined acceptance criteria. To ensure continuous quality of the software, automatic testing with GUI (graphical user interface) and Non-GUI based-tests are performed to cover the software's functionality. The basis for the test automation is described in the corresponding Test Specifications. The matching of automated test cases and test results is ensured through code reviews of the automation scripts.

10. Safety and Effectiveness Information:

Software specifications, design descriptions, hazard analysis, and labeling information are submitted in support of this premarket notification. The device labeling contains instructions for use with cautions to provide for safe and effective use of the device.

The results of the hazard analysis combined with the appropriate preventive measures taken indicate the device is of moderate level of concern, as per the Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (May 11, 2005).

11. Conclusion as to Substantial Equivalence:

The *syngo*.CT Lung CAD is substantially equivalent, both in intended use and indication for use to the following device. The new version has the same basic technical characteristics as the predicate; however, the fundamental technology has been replaced by deep

learning technology. Specifically, the predicate VC20 uses feature-based ML CADe compared to current VC30 deep CNN-based CADe. This does not introduce new types of safety or effectiveness questions. As demonstrated by the statistical analysis and results of the standalone benchmark evaluations:

i. the standalone accuracy has been shown not only to be non-inferior but actually superior to that of the device and
ii. the marks generated by the two devices have been shown to be reasonably consistent.

In summary, Siemens is of the opinion that the *syngo*.CT Lung CAD software, as described within this document, does not pose any unmitigated safety risks and is substantially equivalent to the predicate device since its accuracy has been shown to be superior to the predicate device and the marks are reasonably consistent .

The difference between the predicate device *syngo.CT* Lung CAD VC20 and *syngo*.CT Lung CAD VC30 are minor in nature and both devices have the same characteristics and functionalities.