August 30, 2024

Siemens Medical Solutions USA, Inc.
Clayton Ginn
Official Correspondent
2501 North Barrington Road
Hoffman Estates, Illinois 60192

Re: K242275
Trade/Device Name: syngo.via MI Workflows; Scenium; syngo MBF
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management And Processing System
Regulatory Class: Class II
Product Code: QIH
Dated: August 1, 2024
Received: August 1, 2024

Dear Clayton Ginn:

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.

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,

Daniel M. Krainak, Ph.D.
Assistant Director
DHT8C: Division of Radiological
Imaging and Radiation Therapy Devices
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)*

k242275

Device Name

syngo.via MI Workflows;
Scenium;
syngo MBF

Indications for Use *(Describe)*

syngo.via molecular imaging (MI) workflows comprise medical diagnostic applications for viewing, manipulation, quantification, analysis and comparison of medical images from single or multiple imaging modalities with one or more time-points. These workflows support functional data, such as positron emission tomography (PET) or nuclear medicine (NM), as well as anatomical datasets, such as computed tomography (CT) or magnetic resonance (MR). syngo.via MI workflows can perform harmonization of SUV (PET) across different PET systems or different PET reconstruction methods.

syngo.via MI workflows are intended to be utilized by appropriately trained health care professionals to aid in the management of diseases, including those associated with oncology, cardiology, neurology, and organ function. The images and results produced by the syngo.via MI workflows can also be used by the physician to aid in radiotherapy treatment planning.

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

1. Identification of the Submitter

Submitter / Primary Contact Person	Clayton Ginn Regulatory Affairs clayton.ginn@siemens-healthineers.com +1 (865) 898-2692
Secondary Contact Person	Brian Wui Regulatory Affairs hansong.wui@siemens-healthineers.com +1 (865) 367-4337
Applicant Name and Address	Siemens Medical Solutions, Inc. USA 2501 North Barrington Road Hoffman Estates IL, 60192, USA Establishment Registration Number: 1423253

2. Device Name and Classification

Product Trace Name:	*syngo.*via MI Workflows; Scenium; syngo MBF
Regulation Name:	Medical image management and processing system
Classification Name:	Automated Radiological Image Processing Software
Classification Panel:	Radiology
CFR Section:	21 CFR §892.2050
Device Class:	Class II
Product Code:	QIH

3. Predicate Devices

Primary Predicate Device:

Product Trace Name:	*syngo.*via MI Workflows; Scenium; syngo MBF
510(k) Number:	K232000
Clearance Date:	11/28/2023
Regulation Name:	Medical image management and processing system
Classification Name:	Automated Radiological Image Processing Software
Classification Panel:	Radiology
CFR Section:	21 CFR §892.2050
Device Class:	Class II
Product Code:	QIH

4. Device Description

*syngo.*via MI Workflows (including Scenium and syngo MBF applications) is a multi-modality post-processing software only medical device intended to aid in the management of diseases, including those associated with oncology, cardiology, neurology, and organ function. The *syngo.*via MI Workflows applications are part of a larger *syngo.*via client/server system which is intended to be installed on common IT hardware. The hardware itself is not seen as part of the *syngo.*via MI Workflows medical device.

The *syngo.*via MI Workflows software addresses the needs of the following typical users of the product:

- Reading Physician / Radiologist – Reading physicians are doctors who are trained in interpreting patient scans from PET, SPECT and other modality scanners. They are highly detail oriented and analyze the acquired images for abnormalities, enabling ordering physicians to accurately diagnose and treat scanned patients. Reading physicians serve as a liaison between the ordering physician and the technologists, working closely with both.
- Technologist – Nuclear medicine technologists operate nuclear medicine scanners such as PET and SPECT to produce images of specific areas and states of a patient's anatomy by administering radiopharmaceuticals to patients orally or via injection. In addition to administering the scan, the technologist must properly select the scan protocol, keep the patient calm and relaxed, monitor the patient's physical health during the protocol and evaluate the quality of the images. Technologists work very closely with physicians, providing them with quality-checked scan images.

The software has been designed to integrate the clinical workflow for the above users into a server-based system that is consistent in design and look with the base *syngo.*via platform and other *syngo.*via software applications. This ensures a similar look and feel for radiologists that may review multiple types of studies from imaging modalities other than Molecular Imaging, such as MR.

The *syngo.*via MI workflows software supports integration through DICOM transfers of positron emission tomography (PET) or nuclear medicine (NM) data, as well as anatomical datasets, such as computed tomography (CT) or magnetic resonance (MR).

Although data is automatically imported into the server based on predefined configurations through the hospital IT system, data can also be manually imported from external media, including CD, external mass storage devices, etc.

The Siemens *syngo.*via platform and the applications that reside on it, including *syngo.*via MI Workflows, are distributed via electronic medium. The Instructions for Use is also delivered via electronic medium.

*syngo.*via MI Workflows includes 2 workflows (*syngo.*MM Oncology and *syngo.*MI General) as well as the Scenium neurology software application and the syngo MBF cardiology software application which are launched from the OpenApps framework within the MI General workflow.

5. Indications for Use

*syngo.*via molecular imaging (MI) workflows comprise medical diagnostic applications for viewing, manipulation, quantification, analysis and comparison of medical images from single or multiple imaging modalities with one or more time-points. These workflows support functional data, such as positron emission tomography (PET) or nuclear medicine (NM), as well as anatomical datasets, such as computed tomography (CT) or magnetic resonance (MR). *syngo.*via MI workflows can perform harmonization of SUV (PET) across different PET systems or different PET reconstruction methods.

*syngo.*via MI workflows are intended to be utilized by appropriately trained health care professionals to aid in the management of diseases, including those associated with oncology, cardiology, neurology, and organ function. The images and results produced by the *syngo.*via MI workflows can also be used by the physician to aid in radiotherapy treatment planning.

6. Indications for Use Comparison to the Predicate Device

The indications for use are the same between the subject device and the primary predicate device.

7. Comparison of Technological Characteristics with the Predicate Device

*syngo.*via MI Workflows with software version VB80A, Scenium with software version VE70, and syngo MBF with software version VB30 software provide the same technological characteristics in terms of materials, energy source, and control mechanisms when compared to the legally marketed predicate device since all devices are software only devices.

The software features have been modified in comparison to the predicate device to support enhanced device functionality.

The intended use, indications for use, and fundamental scientific technology for the subject device remains unchanged from the predicate device. No features present from the predicate device have been de-scoped.

At a high level, the subject and predicate devices are based on the following same technological elements:

- Data Supported (PET, SPECT, CT, MR)
- Server/Client architecture
- Workflow Activities (preprocessing, evaluation and reading, reporting and storage)
- Feature Licensing Structure
- SUV values calculated

The following technological differences exist between the subject device and predicate devices.

*syngo.*via MI Workflows VB80:

MI General

- No changes

MM Onco

- No changes

Scenium VE70:

- Centiloid scoring is implemented and intended to standardize brain PET Amyloid quantification across all three approved tracers below.[1]
    - Amyvid™ (florbetapir)
    - Neuraceq™ (florbetaben)
    - Vizamyl™ (flutemetamol)

syngo MBF VB30:

- No changes

Any differences in technological characteristics do not raise different questions of safety and effectiveness. Testing and validation are completed. Test results show that the subject devices are comparable to the predicate devices in terms of technological characteristics and safety and effectiveness and therefore are substantially equivalent to the predicate devices.

8. Non-Clinical and/or Clinical Test Summary & Conclusions

The following performance data were provided in support of the substantial equivalence determination.

Software Verification and Validation

'Enhanced' software documentation per FDA's guidance document "Content of Premarket Submissions for Device Software Functions" issued in June, 2023 is also included as part of this submission. The performance data demonstrates continued conformance with special controls for medical devices containing software. The testing supports that all software specifications have met the acceptance criteria. Verification and validation testing substantiates all requirement and functional specifications, including specifications related to device hazards, and supports the claim of substantial equivalence.

[1] Klunk, William E et al. "The Centiloid Project: standardizing quantitative amyloid plaque estimation by PET." *Alzheimer's & dementia : the journal of the Alzheimer's Association* vol. 11,1 (2015): 1-15.e1-4. doi:10.1016/j.jalz.2014.07.003

Performance Testing

In addition to verification and validation testing, clinical performance evaluation was conducted in order to compare the Centiloid score values generated by Scenium with the Centiloid score values calculated using ADNI[2].

To derive the Scenium SUVr to CL transformation equations, calibration of PET images and their corresponding SUVr and CL reference data were obtained from the GAAIN website. For each tracer, level-2 calibration analysis prescribed in Klunk et al[1]. was performed to generate direct syngo-Aβ SUVr-to-CL transformations. A global cortical SUVr value was calculated using six tracer-specific cortical regions in reference to the whole cerebellum, as implemented in syngo-Aβ software. The transformation equations derived using the calibration images, from GAAIN, fulfilled the acceptance criteria, with strong agreement and little bias between syngo-Aβ CL values and those computed and published using the standard method[1], with

- R^2=0.97(Amyvid™)
- R^2=0.98 (Neuraceq™)
- R^2=0.95 (Vizamyl™)

The independent validation[2] demonstrated strong agreement between syngo-Aβ and ADNI CL values with the following regressions and R^2 values:

- $^{Scenium}CL = 1.044 \times {}^{ADNI}CL - 0.712$; $R^2 = 0.97$ (Amyvid™)
- $^{Scenium}CL = 1.095 \times {}^{ADNI}CL - 7.241$; $R^2 = 0.98$ (Neuraceq™)

Additionally, the agreement of Scenium Centiloid scale with visual reading and progression of disease was investigated[3].162 patients (69 females, 93 males) aged 71.3±6.2 years with Mild Cognitive Impairment (MCI) who underwent an A-PET (22 18F-florbetaben, 52 18F-flutemetamol, 88 18F-florbetapir) were retrospectively reviewed. Patients were classified as “positive” or “negative” by consensus. The ROC analysis yielded excellent agreement with visual-based classification with an area under the ROC curve of 0.9872, and a corresponding optimal CL cut-off value of 26 (sensitivity 92.0%, specificity 96.3%)

Conclusion: We have successfully calibrated a commercially available amyloid quantification software to the centiloid scale for the three commercially available amyloid tracers. Validation on two independent datasets showed strong agreement with the ADNI calibration pipeline for florbetapir and florbetaben. Finally, Centiloid Scoring used by Scenium demonstrated strong agreement with visual reading.

[2] Rachid Fahmi, “Centiloid Calibration of a Commercial Amyloid Quantitation Software for different Fluorine-18 Radiotracers”. EANM 2023.

[3] K. Hirschmüller et al., “Visual Reading and Centiloid Scaling for the Evaluation of Brain Amyloid PET Imaging in Patients with Mild Cognitive Impairment: Impact on Conversion to Alzheimer´s Disease Dementia”. EANM2024.

Risk Analysis

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 of the device was found acceptable to support the claims of substantial equivalence.

Standards

Siemens hereby certifies that *syngo.*via MI Workflows, Scenium, and syngo MBF meets the following FDA Recognized Consensus standards listed below:

Recognition Number	Designation Number and Edition/Date	Title	Standards Development Organization
12-349	PS 3.1 - 3.20 2022d	Digital Imaging and Communications in Medicine (DICOM) Set	NEMA
13-79	62304 Edition 1.1 2015-06 CONSOLIDATED VERSION	Medical Device Software –Software Life Cycle Processes	AAMI, ANSI, IEC
5-125	14971 Third Edition 2019-12	Medical devices – Application of risk management to medical devices	ISO
5-129	62366-1 Edition 1.1 2020-06 CONSOLIDATED VERSION	Medical devices - Part 1: Application of usability engineering to medical devices	AAMI, ANSI, IEC
5-134	15223-1 Fourth edition 2021-07	Medical devices - Symbols to be used with medical device labels, labelling, and information to be supplied - Part 1: General requirements	ISO
5-135	20417 First edition 2021-04 Corrected version 2021-12	Medical devices – Information to be supplied by the manufacturer	ISO

Conclusion

There are no differences in the Indications for Use, Intended Use, or Fundamental Technological Characteristics of the updated *syngo*.via MI Workflows software (including Scenium and syngo MBF) as compared to the currently commercially available *syngo*.via MI Workflows software (K232000).

Both the current and predicate devices are used for viewing, manipulation, quantification, analysis, and comparison of medical images from single or multiple imaging modalities with one or more time-points.

Additionally, the new features implemented within this release do not raise any new issues of safety and effectiveness as compared to the predicate device. Based on this information, as well as the documentation in support of the modifications, it is Siemens' opinion that the *syngo*.via MI Workflows software—with the modifications outlined in this application—is substantially equivalent to the predicate device.