March 5, 2025

Siemens Healthcare GmbH
Abhineet Johri
Regulatory Affairs Manager
Henkestr. 127
Erlangen, 91052
Germany

Re: K241770
Trade/Device Name: Prostate MR AI (VA10A)
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological Computer Assisted Detection And Diagnosis Software
Regulatory Class: Class II
Product Code: QDQ
Dated: February 6, 2025
Received: February 6, 2025

Dear Abhineet 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 (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,

Daniel M. Krainak, Ph.D
Assistant Director
Magnetic Resonance and Nuclear Medicine Team
DHT8C: Division of Radiological
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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.

510(k) Number *(if known)*
K241770

Device Name
Prostate MR AI (VA10A)

Indications for Use *(Describe)*
Prostate MR AI is a plug-in Radiological Computer Assisted Detection and Diagnosis Software device intended to be used
• with a separate hosting application
• as a concurrent reading aid to assist radiologists in the interpretation of a prostate MRI examination acquired according to the PI-RADS standard
• in adult men (40 years and older) with suspected cancer in treatment naïve prostate glands

The plug-in software analyzes non-contrast T2 weighted (T2W) and diffusion weighted image (DWI) series to segment the prostate gland and to provide an automatic detection and segmentation of regions suspicious for cancer. For each suspicious region detected, the algorithm moreover provides a lesion Score, by way of PI-RADS interpretation suggestion.

Outputs of the device should be interpreted consistently with ACR recommendations using all available MR data (e.g., dynamic contrast enhanced images [if available]).

Patient management decisions should not be made solely based on analysis by the Prostate MR AI algorithm.

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.

510(k) Summary

K241770

Prostate MR AI (VA10A)

In accordance with 21 CFR §807.92, the following summary of safety and effectiveness is provided.

I. SUBMITTER

21CFR § 807.92(a)(1)

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Contact: Mr. Abhineet Johri
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Date Prepared: May 17, 2024

II. DEVICE

21CFR § 807.92(a)(2)

Device Trade Name	Prostate MR AI (VA10A)
Classification Name	Radiological Computer Assisted Detection/Diagnosis Software For Lesions Suspicious For Cancer
Device Classification Panel	Radiology
Regulation Number	892.2090
Product Code	QDQ

III. LEGALLY MARKETED PREDICATE DEVICES

21CFR § 807.92(a)(3)

Predicate Device

Device Trade Name	Transpara™
510(k) Number	K181704
Regulation Number	892.2090
Product Code	QDQ

This predicate has not been subject to a design-related recall.

Reference Device

Device Trade Name	ProstatID™

510(k) Number	K212783
Regulation Number	892.2090
Product Code	QDQ

This predicate has not been subject to a design-related recall.

IV. DEVICE DESCRIPTION SUMMARY

21CFR § 807.92(a)(4)

This premarket notification addresses the Siemens Healthineers Prostate MR AI (VA10A) Radiological Computer Assisted Detection and Diagnosis Software (CADe/CADx).

Prostate MR AI is a Computer Assisted Detection and Diagnosis algorithm designed to plug into a hosting workflow that assists radiologists in the detection of suspicious lesions and their classification. It is used as a concurrent reading aid to assist radiologists in the interpretation of a prostate MRI examination acquired according to the PI-RADS standard.

The automatic lesion detection requires transversal T2W and DWI series as inputs. The device automatically exports a list of detected prostate regions that are suspicious for cancer (each list entry consists of contours and a classification by Score and Level of Suspicion (LoS)), a computed suspicion map, and a per-case LoS. The results of the Prostate MR AI plug-in (with the case-level LoS, lesion center points, lesion diameters, lesion ADC median, lesion 10th percentile, suspicion map, and non-PZ segmentation considered optional) are to be shown in a hosting application that allows the radiologist to view the original case, as well as confirm, reject, or edit lesion candidates with their contours and Scores as generated by the Prostate MR AI plug-in. Moreover, the radiologist can add lesions with contours and PI-RADS scores and finalize the case. In addition, the outputs include an automatically computed prostate segmentation, as well as sub-segmentations of the peripheral zone and the rest of the prostate (non-PZ).

The algorithm will augment the prostate workflow of currently cleared *syngo*.MR General Engine if activated via a separate license on the General Engine.

V. INTENDED USE/INDICATIONS FOR USE

21CFR § 807.92(a)(5)

Indications for Use Comparison

Predicate Device **Transpara™** **K181704**	**Reference Device** **ProstatID™** **K212783**	**Subject Device** **Prostate MR AI (VA10A)**
The ScreenPoint Transpara™ system is intended for use as a concurrent reading aid for physicians interpreting screening mammograms, to identify regions suspicious for breast cancer and assess their likelihood of malignancy. Output of the device includes marks placed on suspicious soft tissue lesions and suspicious calcifications; region-based scores, displayed upon the physician's query, indicating the	ProstatID™ is a radiological computer assisted detection (CADe) and diagnostic (CADx) software device for use in a healthcare facility or hospital to assist trained radiologists in the detection, assessment and characterization of prostate abnormalities, including cancer lesions using MR image data	Prostate MR AI is a plug-in Radiological Computer Assisted Detection and Diagnosis Software device intended to be used • with a separate hosting application • as a concurrent reading aid to assist radiologists in the interpretation of a prostate MRI examination acquired

likelihood that cancer is present in specific regions; and an overall score indicating the likelihood that cancer is present on the mammogram. Patient management decisions should not be made solely on the basis of analysis by Transpara™.	with the following indications for use. ProstatID analyzes T2W, DWI and ADC MRI data. ProstatID does not include DCE images in its analysis. ProstatID software is intended for use as a concurrent reading aid for physicians interpreting prostate MRI exams of patients presented for high-risk screening or diagnostic imaging, from compatible MRI systems, to identify regions suspicious for prostate cancer and assess their likelihood of malignancy. Outputs of the device include the volume of the prostate and locations, as well as the extent of suspect lesions, with index scores indicating the likelihood that cancer is present, as well as an exam score by way of PI-RADS interpretation suggestion. "Extent of suspect lesions" refers to both the assessment of the boundary of a particular abnormality, as well as identification of multiple abnormalities. In cases where multiple abnormalities are present, ProstatID can be used to assess each abnormality independently. Outputs of this device should be interpreted with all available MR data consistent with ACR clinical recommendations (e.g., dynamic contract enhanced images if available) in context of PI-RADs v2, and in conjunction with bi-parametric MRI acquired with either surface or endorectal MRI accessory coils from compatible MRI systems. Analysis by ProstatID is not	according to the PI-RADS standard • in adult men (40 years and older) with suspected cancer in treatment naïve prostate glands The plug-in software analyzes non-contrast T2 weighted (T2W) and diffusion weighted image (DWI) series to segment the prostate gland and to provide an automatic detection and segmentation of regions suspicious for cancer. For each suspicious region detected, the algorithm moreover provides a lesion Score, by way of PI-RADS interpretation suggestion. Outputs of the device should be interpreted consistently with ACR recommendations using all available MR data (e.g., dynamic contrast-enhanced images [if available]). Patient management decisions should not be made solely based on analysis by the Prostate MR AI algorithm.

	intended as a replacement for interpreting prostate abnormalities using MR image data consistent with clinical recommendations (including DCE); nor should patient management decisions be made solely on the basis of ProstatID.	

The indication for Use of Prostate MR AI is similar to that of the predicate device. Both devices are designed for use by medical professionals who analyze radiological images, assisting them in pinpointing and characterizing abnormalities. The devices are both intended to be used concurrently with image interpretation but are not meant to replace a clinician's evaluation or clinical judgement. Thus, the subject and predicate devices are both intended to perform the same type of function and serve the same fundamental role in medical practice.

There are distinctions in the disease-specific abnormalities these devices can identify, the types of medical images they can process, and the specific patient populations they are intended for. The core functionalities of lesion identification and interpretation for medical images remain consistent across the differences. The new concerns regarding the safety and effectiveness of the device raised by these distinctions are assessed and resolved in the device designs to ensure the substantial equivalence.

Indications for Use/Intended Use Comparison Summary and Conclusion

The Indications for Use were assessed in accordance with the following FDA Guidance Documents:

- The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]

The results of this evaluation determined that the Indications for Use for the subject device and the predicate device are fundamentally equivalent, and only include differences in modality type, body region, and vendors. As such, Siemens Healthineers is of the opinion that the Intended Use and Indications for Use are similar to the predicate device.

VI. COMPARISON OF FEATURES AND SPECIFICATIONS WITH THE PREDICATE DEVICES

21CFR § 807.92(a)(6)

Attribute	Predicate Device Transpara™ K181704	Reference Device ProstatID™ K212783	Subject Device Prostate MR AI (VA10A)	Equivalency Analysis
General Information				
Regulation number	§ 892.2090 Radiological Computer Assisted Detection and Diagnosis Software	§ 892.2090 Radiological Computer Assisted Detection and Diagnosis Software	§ 892.2090 Radiological Computer Assisted Detection and Diagnosis Software	Identical
Classification	Class II	Class II	Class II	Identical
Product Code	QDQ	QDQ	QDQ	Identical
Clinical Characteristics				

Attribute	Predicate Device Transpara™ K181704	Reference Device ProstatID™ K212783	Subject Device Prostate MR AI (VA10A)	Equivalency Analysis
Intended Use (short)	A concurrent reading aid for physicians interpreting screening FFDM acquired with compatible mammography systems, to identify findings and assess their level of suspicion.	A concurrent reading aid for physicians interpreting prostate MRI exams of patients presented for high-risk screening or diagnostic imaging, to identify regions suspicious for prostate cancer and assess their likelihood of malignancy.	A concurrent reading aid for physicians interpreting prostate MRI examinations acquired according to the PI-RADS standard, to identify findings and assess their level of suspicion.	Equivalent – Justified in Section V.
Intended patient population	Women undergoing screening mammography	Population of biological males with a prostate gland undergoing screening or clinical MRI exams. This includes biological males of all ages with clinical indicators suggestive of possible prostate cancer or with family history of prostate cancer.	Adult men (40 years and older) with suspected prostate cancer undergoing prostate MRI without prior treatment of the prostate gland (treatment-naïve).	Equivalent – Images captured from different patient populations are standardized to be processible by CAD devices.
Anatomical region of interest	Breast	Prostate gland	Prostate gland	Equivalent – Images captured from different anatomical regions are standardized to be processible by CAD devices.
Intended Users	physicians qualified to read screening mammograms	Physicians qualified to read and interpret prostate MRI exams consistent with ACR recommendations in the context of PI-RADS v2	Radiologists qualified to read prostate MRI	Equivalent – – Users are qualified to read radiology images using CAD devices
Mode of action	Software that applies algorithms for recognition of suspicious calcifications and soft tissue lesions to detect and characterize findings in radiological breast images and provide information about the presence, location, and characteristics of the findings to the user.	Software that applies algorithms for recognition of suspicious tissue regions in Prostate MR images to provide information about the presence, location, and level of suspicion of the findings.	Software that applies algorithms for recognition of suspicious tissue regions in Prostate MR images to provide information about the presence, location, and level of suspicion of the findings.	Equivalent – Both predicate and subject devices use algorithms to detect findings and provide diagnosis.
Medthod of Use	Concurrent	Concurrent	Concurrent	Identical

Attribute	Predicate Device Transpara™ K181704	Reference Device ProstatID™ K212783	Subject Device Prostate MR AI (VA10A)	Equivalency Analysis
Visualization Features	Computer aided detection (CAD) marks to highlight locations where the device detected suspicious calcifications or soft tissue lesions. Decision support is provided by region scores on a scale ranging from 0-100, with higher scores indicating a higher level of suspicion.	ProstatID does not include a standalone graphical user interface. Rather, ProstatID outputs are in DICOM format and may be viewed on DICOM-compliant image viewers.	Prostate MR AI does not include a standalone graphical user interface. Rather, it is a plug-in device that is intended to be used with a separate hosting application that allows the user to view the original case, as well as confirm, reject, edit, or add lesions, their contours and Scores.	Equivalent – The difference between predicate and subject devices is justified by using the reference device which also does not have UI while it retains the same level of safety and effectiveness.
Technical Characteristics				
Design	Software only device	Software only device	Software only device	Identical
Automatic Segmentation	Yes	Yes	Yes	Identical
Algorithm	Artificial intelligence algorithm trained with large datasets of biopsy proven examples of breast cancer, benign lesions and normal tissue.	Neural network trained on a database of reference normal tissues and abnormalities with known ground truth.	Artificial intelligence algorithm trained on a database of prostate MR image series acquired according to the PI-RADS standard (non-contrast T2W and DWI image series), and corresponding radiological and/or biopsy findings.	Identical – all trained AI algorithms
Alteration original image	No	No	No	Identical
Data acquisition protocol	Screening mammograms	Prostate MRI image series	Prostate MRI image series acquired according to the PI-RADS standard	Equivalent – Acquired images are qualified for CAD device processing
Input	Medical images provided in a DICOM format	Medical images provided in a DICOM format	Medical images provided in a DICOM format	Equivalent – Devices all use standardized image types.

Attribute	Predicate Device Transpara™ K181704	Reference Device ProstatID™ K212783	Subject Device Prostate MR AI (VA10A)	Equivalency Analysis
Output	• Marks placed on suspicious soft tissue lesions and suspicious calcifications • Region-based scores indicating the likelihood that cancer is present • Overall score indicating the likelihoood that cancer is present on the mammogram	• Marks locations suspicious of lesions • Provides region scores with higher scores indicating a higher level of suspicion • Provides single exam score that synthesizes features	• Automatically segments the contours of the prostate gland • Automatically segments the parts of the prostate that belong to the periheral zone (PZ) and that do not belong to the peripheral zone (non-PZ), respectively • Calculation of a "Suspicion Map" that indicates lesions suspicious for cancer • For each detected lesion: o Lesion contours o Rating of severity ("Score") on a scale from 3 to 5 (in steps of 1). Score is generated by an algorithm trained on the correlation of prostate MRI with PI-RADS scores provided by radiologists and results of lesion-targeted biopsy. o A "Level of Suspicion" (LoS) on a scale from 60 to 100 (in steps of 1) as a fine granular measure of the algorithm's suspicion for the presence of a significant lesion, based on training on PI-RADS scores provided by radiologists and results of lesion-targeted biopsy	Equivalent – as far as the different body regions allow. PZ vs. non-PZ is prostate specific and is relevant for PI-RADS evaluation. Instead of marks for suspicious locations in the image, the subject device provides lesion contours and a "suspicion map".

Attribute	Predicate Device Transpara™ K181704	Reference Device ProstatID™ K212783	Subject Device Prostate MR AI (VA10A)	Equivalency Analysis
Score	Finding level: Continuous score 1-100 indicating the level of suspicion of malignancy (from low suspicion to high suspicion). Breast level: None Exam level: 10-point scale score indicative of higher frequency of cancer positive	Finding level: Scores on a continuous scale from 0 to 1 that accompany the overlay markings of suspicious locations Case level: Suggested level of suspicion (LoS) or overall PI-RADS exam score	Finding level: Rating of severity ("Score") on a scale from 3 to 5 (in steps of 1). The Score is generated by an algorithm trained on the correlation of prostate MRI with PI-RADS scores provided by radiologists and results of lesion-targeted biopsy A "Level of Suspicion" (LoS) on a scale from 60 to 100 (in steps of 1) as a more granular measure of the algorithm's suspicion for the presence of a significant lesion, based on training on PI-RADS scores provided by radiologists and results of lesion-targeted biopsy Prostate level (= Exam Level): LoS derived from Finding Level results as maximum LoS over all findings (on a scale of 60-100 in steps of 1), or (in the absence of findings) as maximum of internal Suspicion Map over prostate segmentation (on a scale of 1-59 in steps of 1)	Equivalent – The differences between predicate and subject devices can be justified by using the reference device which apply continuous finding scale and share the same PI-RADS LoS exam score.
Finding discovery	Findings are by-default displayed when score is equal or higher than 5. Upon user request for findings of score equal or less than 4.	Findings are added to post-processed T2W image in DICOM format as a colorized translucent overlay to highlight locations, as overlay scores on a continuous scale from 0 to 1, and as a suggested LoS or overall PI-RADS exam score.	Upon activation of the plug-in, findings are displayed in the hosting workflow as segmentations on the T2W image series with corresponding ratings by Scores (value range: 3-5), and as an overall exam Score.	Equivalent – Finding results of both predicate and subject devices can be displayed.

Attribute	Predicate Device Transpara™ K181704	Reference Device ProstatID™ K212783	Subject Device Prostate MR AI (VA10A)	Equivalency Analysis
Performance	Reader study with 6720 reads: • fully crossed multi-reader, multi-case design • 240 cases • 14 radiologists **Case-level ROC:** • radiologists' AUC unaided = 0.866 • radiologists' AUC aided = 0.886 • mean difference: +0.020, 95% C.I. [0.010, 0.030]	Reader study with 2700 reads: • 150 cases were read by 9 trained physicians in two separate reads – first without ProstatID, and second with ProstatID. **Case-level ROC** for discriminating Gleason Score ≥ 7 in those 130 out of the 150 cases that had biopsy results: • radiologists' AUC unaided = 0.629 • radiologists' AUC unaided = 0.671 • mean difference: +0.042, 95% C.I. [0.005, 0.080] **Lesion-level wAFROC:** • radiologists' AUC unaided = 0.387 • radiologists' AUC aided = 0.430 • mean difference: +0.043, 95% C.I. [0.003, 0.083]	Reader study with 4080 reads: • split-plot multi-reader, multi-case design (comprising 2 fully crossed multi-reader, multi-case splits) • 2× 170 = 340 cases from 2 consecutively acquired cohorts • 2× 6 = 12 radiologists • Two analysis scenarios: a) all cases, all readers b) only cases with biopsy, or a negative MRI and ≥12 months negative follow-up by PSA or MRI (exclusion of 34 cases), and only case-reader pairs in which readers were not involved in prostate MRI reading at the institution providing the case during the time of data collection (exclusion of 459 case-reader pairs) **Case-level ROC** for discriminating Gleason Score ≥ 6: • radiologists' AUC (unaided) = a) 0.676; b) 0.658 • radiologists' AUC (aided) = a) 0.701; b) 0.695 • mean difference: a) +0.025, 95% C.I. [0.001, 0.049] b) +0.037, 95% C.I. [0.011, 0.063] **Lesion-level wAFROC:** • radiologists' AUC unaided = a) 0.734; b) 0.772 • radiologists' AUC aided = a) 0.769; b) 0.834 • mean difference: a) +0.035, 95% C.I. [0.002, 0.068] b) +0.030, 95% C.I. [0.008, 0.052]	Equivalent – The difference between the predicate and subject devices can be justified by comparing with the performance of the reference device. Reader studies of both reference and subject devices used similar statistically meaningful case numbers, qualified readers, acceptance criteria and yielded comparable study results.

The predicate and subject devices are both Computer Assisted Detection and Diagnosis Software devices to assist radiologists to detect and diagnose diseases based on the radiological images. They share

significant similarities in the functionalities of detection, assessment and characterization of human tissue abnormalities on radiological images using AI/ML augmented technologies.

While technological characteristics of the predicate device Transpara™, e.g., network architecture and training process, remain unknown to the public, the verification and validation testing of the subject device Prostate MR AI demonstrate that the device can perform prostate gland segmentation, lesion detection and classification as intended, meeting all the design inputs. The risks associated with the algorithm development are mitigated as far as possible. The detection and diagnosis accuracy of the subject device was assessed to validate the appropriateness and implementation of the intended use. In addition, a Multi-Reader/Multi-Case Study was performed to demonstrate that radiological reading aided by Prostate MR AI yields better diagnostic performance than unaided reading. Evidence provided within this submission demonstrates conformance with special controls for software as medical devices. The differences in technological characteristics between the subject device Prostate MR AI and the predicate device do not constitute any new intended use and do not raise new questions of safety and effectiveness.

The other differences between the subject device and the predicate device, notably the body regions targeted, are justified based on the reference device ProstatID™.

In summary, Siemens is of the opinion that Prostate MR AI (VA10A) does not raise new or different questions of safety or effectiveness and is substantially equivalent to the currently marketed predicate device Transpara™ (K181704).

VII. PERFORMANCE DATA

The following performance data were provided in support to demonstrate similarities to the predicate / previously cleared device.

Summary of Software Verification and Validation

No performance standards for CADe/CADx have been issued under the authority of Section 514. Non-clinical testing was conducted for the device Prostate MR AI (VA10A) during product development. The features described in this Premarket Notification were supported with verification and validation testing.

Siemens Healthineers claims conformance to the following recognized consensus standards:

- ISO 14971 Third Edition 2019-12
- IEC 62304 Edition 1.1 2015-06 CONSOLIDATED VERSION
- IEC 82304-1 Edition 1.0 2016-10

Software documentation for Basic Documentation Level per FDA's Guidance Document "Content of Premarket Submissions for Device Software Functions" issued on June 14, 2023 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 Prostate MR AI 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.

Nonclinical Test Summary 21CFR § 807.92(b)(2)

Automatic prostate segmentation

To monitor the performance of the automatic prostate segmentation, an automated test routine was established that compared the segmentation result of 222 transversal T2 series from more than 10 clinical sites against ground truth generated by radiologists. The image data base of this formal test includes ~31% cases acquired with a 1.5T system and ~69% cases acquired with a 3T system. Of the test data 41%, 27%, and 32% were scanned on Siemens, Philips, and GE MR systems, respectively.

The reference standard was established through pixel-wise consensus, which was built based on annotation results of three expert radiologists. Two metrics were used for the evaluation. One was based on the Dice score of pairs of segmentation masks, and the other was based on the normalized volume difference based on the computed volumes of masks.

The overall results demonstrate the following:

- The median of the Dice score between the AI algorithm results and the corresponding ground truth masks exceeds the threshold of 0.9.
- The median of the normalized volume difference between the algorithm results and the corresponding ground truth masks is within a ±5% range.
- The AI algorithm results as compared to any individual reader are statistically non-inferior based on variabilities that existed among the individual readers within the 5% margin of error and 5% significance level.

Prostate lesion detection and classification

To monitor the performance of the automatic prostate lesion detection and classification, an automated test routine was established that compared the result of the automatic lesion detection and classification result for

- 105 cases from 6 sites against a ground truth generated by radiologists,
- 115 cases from 6 sites against a ground truth generated by prostate biopsy, as well as
- 340 cases from the multi-reader multi-case study.

The reference standard for the radiology ground truth was established through consensus reading of three expert radiologists in prostate MRI reading. The reference standard for the pathology ground truth was established through biopsy results for the same patient. Therefore, in the pathology ground truth, only case level annotation was available, while in the radiology ground truth, lesion level annotation was also included. Sensitivity and false positive rate per case was used to evaluate the performance of prostate lesion detection and classification, and accuracy was used to determine the performance of the PI-RADS classification.

The overall results demonstrated the following:

- The case level sensitivity of the lesion detection is equal or greater than 0.80 for both radiology and pathology ground truth.
- The false positive rate per case of the lesion detection is smaller than one false positive per case for radiology ground truth.
- The accuracy of the PI-RADS classification of radiology ground truth lesions detected by the algorithm is equal or greater than 0.8.

- The non-inferior performance of the subject device in GE vs Siemens and African American vs non-African American cases, and in cases with peripheral zone vs non- peripheral lesions

All pre-specified criteria for non-clinical testing were therefore met.

Clinical Test Summary

21CFR § 807.92(b)(2)

For assessment of the clinical performance of the device, a reader study was conducted with the objective to determine whether individual radiologists perform better with than without Prostate MR AI in the task of identifying cases of treatment-naïve men that are suspicious of prostate cancer based on a prostate MRI examination acquired according to the PI-RADS standard. In order to compare the reading performance of radiologists with and without the aid of Prostate MR AI, a study design with independent arms for aided and unaided reading is appropriate to test both reading conditions. The study was set up as a multi-reader multi-case (MRMC) study in a paired split-plot design, which essentially combined two fully-crossed MRMC (sub-)studies conducted in parallel, each using half of the overall readers and half of the overall cases.

Within each of the two MRMC sub-studies, multiple radiologists performed two reads of multiple prostate MRIs, one without and one with the support of Prostate MR AI. Between the sessions there was a wash-out time interval of at least 28 days. All of the 12 Readers were American Board of Radiology certified and selected to reflect a spectrum of experience and practice type background.

Study cases were selected retrospectively to be representative of the population of U.S. men undergoing prostate MRI without prior treatment of the prostate gland.

For inclusion in the reader study, 340 cases were selected. The cases from two US sites were consecutive and not enriched for positive cases. To adequately represent African American patients, who are more likely to be diagnosed with prostate cancer, present at an earlier age, and are more likely to have advanced disease at diagnosis[1], additional consecutive patient cases specifically from men of African descent were included to ensure that at least 13% of the study cases are of Black or African American ethnicity[2].

The cases for the reader study were kept completely separate from those used for the training of the Prostate MR AI algorithm.

The **primary endpoint** of the study was based on the comparison of case-level diagnostic performance of aided and unaided reads using the reader-provided case-level LoS (RLoS), that is, a PI-RADS scale with additional intermediate steps of 0.5. The resulting finer granularity, which is not used in clinical practice, was introduced for improved accuracy of the comparative assessment. Biopsy results (with the criterion Gleason Grade Group GGG greater or equal to 1, i.e. any cancer on biopsy), and in case they were not available, PSA density and follow-up were used to determine the reference standard.

However, as consecutive cases were used in order to avoid selection bias, not all cases had unquestionable ground truth in terms of biopsy information or a negative MRI with negative follow-up of at least 12 months by PSA density or MRI. Therefore, two alternative evaluations were performed in

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[1] Smith ZL, Eggener SE, Murphy AB: African-American Prostate Cancer Disparities. Curr Urol Rep **18**, 81 (2017)

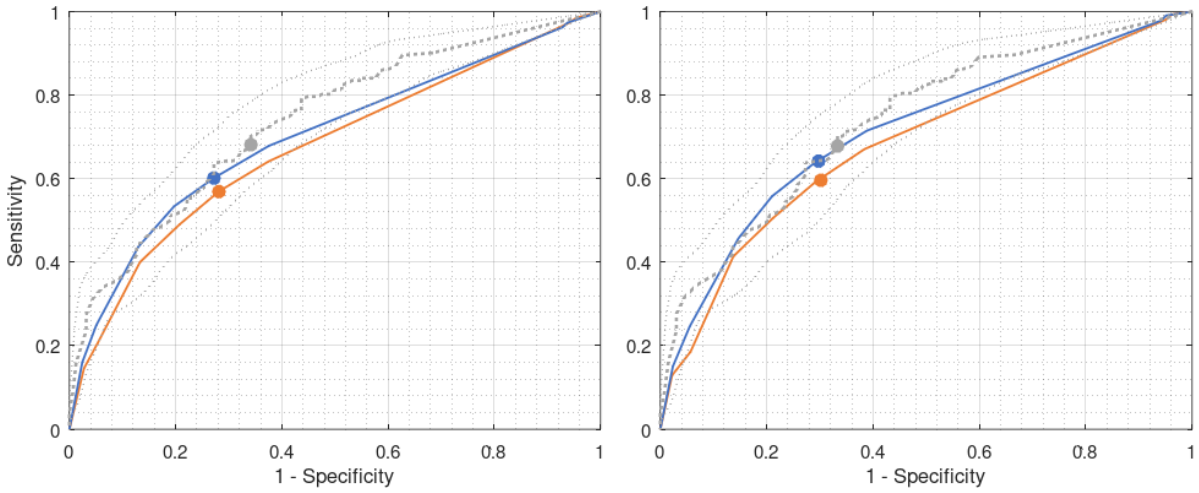
[2] https://www.census.gov/quickfacts/fact/table/US/IPE120219 (accessed on Feb 6th, 2022) gives an estimate of 13.4% for the U.S. population of Black or African American ethnicity for July 1st, 2021

parallel: a *fully inclusive* and a *maximally restrictive* analysis.
In the fully inclusive scenario, all cases and readers were considered, using a probabilistic treatment if definite reference standard labels were not available.
In the maximally restrictive scenario, only cases with biopsy information, or a negative MRI **and** 12-month negative follow-up by PSA density or MRI, were used. Moreover, reader-case pairs were excluded if readers were involved in clinical prostate MRI evaluation at the institution that provided the cases during the period of data collection.

In the fully inclusive analysis, the average area under the ROC (Receiver Operating Characteristic) curve (AUROC) improved from 0.6758 in unaided reading to 0.7010 in aided reading, with a difference of 0.0252 (95% C.I. [0.0011, 0.0493]; *P*=0.040).
In the maximally restrictive analysis, AUROC improved from 0.6579 in unaided reading to 0.6948 in aided reading, with a difference of 0.0368 (95% C.I. [0.0108, 0.0628]; *P*=0.006).

In either analysis, the improvement was statistically significant and the primary endpoint thus met.

The following figures show the pooled ROC curves and RLoS ≥ 3 operating points for the discrimination of any cancer on biopsy (Gleason Grade Group ≥ 1) in unaided (orange) and aided reading (blue). The grey curve denotes AI standalone performance (with 95% confidence interval envelope); left: fully inclusive analysis, right: maximally restrictive analysis.



In the fully inclusive analysis, the average sensitivity/specificity of the Readers at a case-level RLoS threshold of ≥ 3 was 0.57 (95% C.I.: [0.49, 0.64]) / 0.72 (95% C.I. [0.64, 0.79]) in unaided and 0.60 (95% C.I.: [0.53, 0.68]) / 0.73 (95% C.I.: [0.65, 0.80]) in aided reading.

For the **secondary endpoint** (an analysis of the lesion-level reading performance in unaided and aided reading), AUwAFROC (area under the average weighted alternative free receiver operating characteristic) figures of merit were determined, using as reference standard consensus lesions with a consensus PI-RADS of at least 3 from majority voting among 3 experienced radiologists acting as Truthers. Against this, the Readers' corresponding true positives (correct lesion localizations) and false positive lesion detections were held, with their respective ratings.

Although in this analysis the reference standard is not in question for any case, for full equivalence to the primary analysis the evaluation was performed both for the fully inclusive and the maximally restrictive analysis scenario.

In the fully inclusive analysis, AUwAFROC improved in aided vs. unaided reading by 0.0350 (95% C.I.:[0.0020, 0.0681], *P*=0.037).

In the maximally restrictive analysis, AUwAFROC improved in aided vs. unaided reading by 0.302 (95% C.I.: [0.0080,0.0520], *P*=0.008).

In either analysis, the improvement was statistically significant and the secondary endpoint thus met.

In a supplemental analysis for the fully inclusive analysis scenario, Fleiss' Kappa for interreader agreement in per-case PI-RADS scores was 0.283 (95% C.I.: [0.242, 0.322]) for unaided reads, and 0.371 (95% C.I.: [0.326, 0.411]) for aided reads, with a difference of 0.087 (95% C.I. [0.051, 0.125]). The improvement in Fleiss' Kappa between unaided and aided reads was statistically significant (*P*<0.0001).

The device thus passed clinical testing for case-level and lesion-level reading performance improvement in aided vs. unaided reads.

Summary

Performance tests were conducted to test the functionality of the device Prostate MR AI (VA10A). 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.

Safety and Effectiveness Information

Software design description, hazard analysis, and technical and safety information have been completed and provided in support of this device. 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 are included in documentations of Basic Documentation Level, as per Guidance "Content of Premarket Submissions for Device Software Functions", June 2023.

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

VIII. CONCLUSIONS

21CFR § 807.92(b)(3)

In accordance with Guidance Document "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]", the predicate device for this submission is Transpara™, cleared via Premarket Notification K181704 on November 21, 2018.

On the basis of the comparison of device properties provided above including intended use, technological characteristics, performance and risks, Siemens Healthineers believes that the subject device, Prostate MR AI (VA10A) is as safe and effective as and substantially equivalent to the predicate device, Transpara™.