FDA U.S. FOOD & DRUG ADMINISTRATION

EVALUATION OF AUTOMATIC CLASS III DESIGNATION FOR
ArteraAI Prostate
DECISION SUMMARY

I Background Information:

A De Novo Number

DEN240068

B Applicant

Artera Inc.

C Proprietary and Established Names

ArteraAI Prostate

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
SFH	Class II	21 CFR 864.3755 Software algorithm device analyzing digital images for cancer prognosis	88 – PATHOLOGY

II Submission/Device Overview:

A Purpose for Submission:

De Novo request for evaluation of automatic class III designation for ArteraAI Prostate.

B Measurand:

Scanned whole slide images (WSI) of Hematoxylin & Eosin (H&E)-stained prostate needle core biopsies.

C Type of Test:

Evaluation of scanned WSIs of H&E-stained prostate needle biopsies by Artificial Intelligence/Machine Learning (AI/ML) based algorithm to provide cancer associated prognostic 10-year risk estimates of distant metastasis (DM) and prostate cancer specific mortality (PCSM).

III Indications for Use:

A. Indication(s) for Use:

ArteraAI Prostate is a software only device intended to analyze scanned histopathology whole slide images (WSIs) from treatment-naïve prostate core needle biopsies prepared from formalin fixed paraffin-embedded (FFPE) tissue and stained using Hematoxylin & Eosin (H&E) stains. ArteraAI Prostate provides 10-year risks of distant metastasis and prostate cancer specific mortality and is intended to assist physicians with prognostic risk-based decisions along with other clinicopathological factors in non-metastatic prostate cancer patients.

ArteraAI Prostate is intended for males 55 years of age or older without clinically or pathologically defined metastases, and who are candidates for curative intent management (surgery, radiation therapy with or without systemic therapy, or active surveillance).

ArteraAI Prostate is intended to utilize WSIs acquired from an FDA-cleared interoperable scanner with which ArteraAI Prostate has been authorized for use or a 510(k)-cleared scanner that has been assessed in accordance with the Predetermined Change Control Plan (PCCP) for qualifying additional interoperable scanners.

B Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

<u>Warnings</u>

1. The ArteraAI Prostate should be used in conjunction with a complete standard of care evaluation.
2. The ArteraAI Prostate patient report is to be utilized by trained physicians after being released by the pathology laboratory user.
3. The ArteraAI Prostate results correctness is based on the quality requirements of the slide images and appropriate whole slide imaging scanner usage.
4. Ensure proper traceability of the scanned images to the patient using an anonymized patient ID.

Please refer to the labeling for a complete list of warnings and precautions.

C Special Instrument Requirements:

Philips Ultra Fast Scanner (DEN160056)

IV Device/System Characteristics:

A Device Description:

ArteraAI Prostate is a software only device that utilizes deep learning algorithms developed with WSI of H&E-stained prostate needle biopsies to assess risk of distant metastasis and prostate cancer specific mortality. The software performs an algorithmic assessment of features extracted from WSIs using self-supervised learning. ArteraAI Prostate consists of one algorithm, comprised of multiple building block models that intake image data to calculate ArteraAI raw scores. These raw scores are used to estimate risk categories (High, Intermediate, Low) for 10-year risk of DM and PCSM. The algorithm is locked; it is not a continuous learning (continual machine learning model) algorithm.

ArteraAI Prostate includes the ArteraAI Platform (which includes the sub-components ArteraAI Web Portal and ArteraAI Back-End) and ArteraAI Prostate (which includes the sub-components ArteraAI Image Converter and the ArteraAI AI Engine). The ArteraAI Prostate interacts with the ArteraAI Platform. The functions of the above components are provided in the Table 1 below.

Table 1. ArteraAI Prostate Sub-Components Overview

Sub-Component	Description
ArteraAI Platform	
ArteraAI Web Portal	Allows users to interact with the platform to perform the following functions: 1. Select the test to be performed. 2. Input data. 3. Pass data to the Back-End component. 4. Receive report generated for the given patient ID. 5. Manage records from the previously executed tests. 6. Access instructions for use and labeling information. The sub-component does not modify the data or take any action other than transmitting it to the back end.
ArteraAI Back-End	Manages the task execution of other components and performs the following functions: 1. Send and retrieve data associated with a given ID to/from the database. 2. Start Image Converter jobs and pass the location of slide images to the Image Converter.

Sub-Component	Description
ArteraAI Platform	
	3. Start AI jobs and pass location of slide images to the AI Engine. 4. Compile PDF reports. 5. Manage user authentication. The sub-component does not modify the data or take any action other than transmitting it to the AI Engine and Image Converter and populate the PDF report with results from the AI Engine.
ArteraAI Prostate	
ArteraAI Image Converter	Converts images to a format usable by the AI Engine (iSyntax to TIFF).
ArteraAI AI Engine	Includes the AI/ML algorithm and performs the evaluation of WSIs that are uploaded and provides the device output as described in the intended use.

Device Input:
The only input to the device is WSIs of H&E-stained prostate needle biopsy. WSIs are generated from the FDA cleared Philips Ultra Fast Scanner with below Settings:

Magnification: 40x
Resolution: 0.25 µm/pixel
Compression: Proprietary of Philips
File format: iSyntax, Philips proprietary file format with either RAW or iSyntax compression.

All WSIs from prostate cancer biopsy slides with the same highest Gleason grade determined by the pathologist are uploaded to the ArteraAI web portal which are then analyzed by the ArteraAI Prostate device. The ArteraAI Prostate device initially calculates a raw score for a patient. Then two cutoffs C1 and C2 are applied to the raw score for determination of the ArteraAI Prostate risk categories:

Raw Score > C2, then category=High
C1<Raw Score ≤C2, then category=Intermediate
Raw Score ≤C1, then category=Low

The highest ArteraAI Prostate risk category is provided in the patient report.

Device Output:
The test output is a patient specific report, which includes the following:

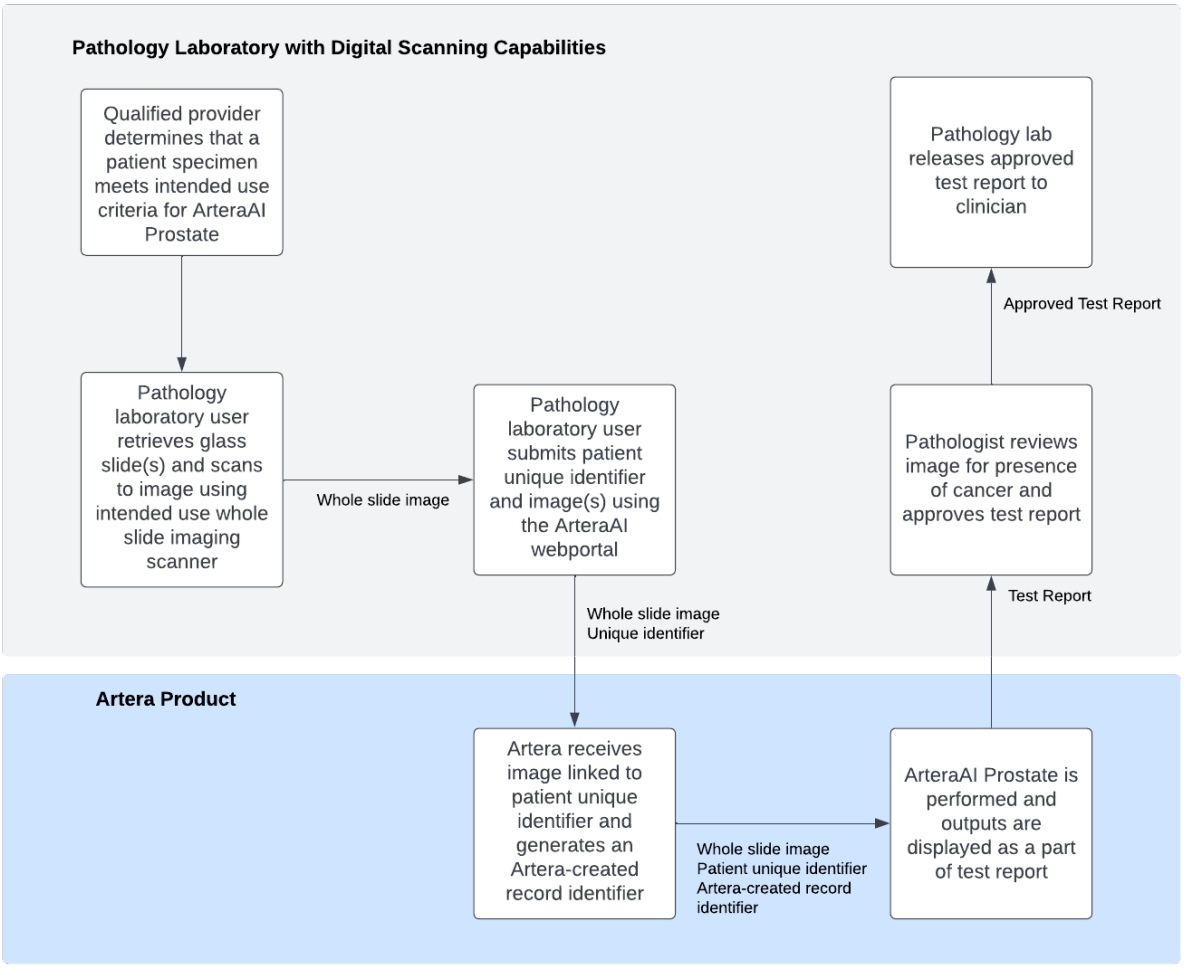
- 10-year ArteraAI Prostate Categorical Risk for Distant Metastasis (High, Intermediate, Low)
- Individual 10-year risk for Distant Metastasis (Low and Intermediate)
- 10-year ArteraAI Prostate Categorical Risk for Prostate Cancer Specific Mortality (PCSM) (High, Intermediate, Low)

The ArteraAI Prostate patient report is intended to be interpreted by the physician to aid in understanding the risk of DM or PCSM in the prostate cancer patient. The results are provided to support risk-based decisions within the recommended professional guidelines.

B Principle of Operation

ArteraAI Prostate is intended to be operated within a pathology laboratory with digital scanning capabilities. The ArteraAI Prostate workflow is depicted in Figure 1 below.

Figure 1. ArteraAI Prostate Workflow



The slide review and image selection procedure for uploading to the ArteraAI web portal is as follows:

1. ArteraAI Prostate is performed on WSI images of prostate core biopsy specimen after a patient's diagnosis of prostate cancer per standard of care. A qualified pathologist must have already determined that prostate cancer is present in the patient prostate core biopsy specimen. ArteraAI Prostate is intended for use only with slide images that contain non-metastatic prostate cancer. If there is no prostate cancer in any of the biopsy cores, ArteraAI Prostate should not be used.
2. The pathologist will identify the WSI(s) of the biopsy specimen containing the highest Gleason score. The WSIs are obtained using the FDA-cleared Philips Ultra Fast scanner at 40x magnification in accordance with the scanner's Instructions for Use.
3. The WSIs are reviewed to verify that the image is not blurry, no defects are present and the whole tissue region is included in the image. Additional image and other related quality control steps are performed per the ArteraAI Prostate Instructions for Use.
4. The WSI(s) and a unique patient identifier are entered as data inputs to the ArteraAI web portal that is then transferred to Artera's back-end infrastructure. The patient identifier is intended to provide end-to-end traceability while protecting patient health information privacy.
5. During the WSI transfer process, a web worker (thread) which is a web browser feature, is used to manage the upload of the WSI to parallelize the data transfer. This allows the image and other data upload to proceed in the background, allowing the operator to continue interacting with the system without interruption.
6. ArteraAI Prostate uses the uploaded WSI(s) as input. Additional clinical data, if entered into the web portal, are not used as an input to ArteraAI Prostate but are only for the purposes of including this information in the ArteraAI Prostate Test Report.
7. ArteraAI Prostate produces a test report that summarizes the ArteraAI Prostate results and transfers the test report to the pathology laboratory via the ArteraAI web portal.
8. The pathologist will confirm the presence of cancer within the uploaded WSI, review and approve the report in accordance with the local laboratory procedures and release the test report to the requesting clinician.

C. ArteraAI Prostate Prognostic Model Development

The AI algorithm used in the ArteraAI Prostate was developed using deep learning machine learning algorithms trained on WSIs of H&E- stained prostate needle biopsy slides from multiple, multi-center, prospective randomized controlled clinical trials and clinical studies to assess 10-year risk of DM and PCSM. As indicated in the Table 2 below the datasets included a representative spectrum of cases with diagnostic variability including a range of Gleason scores, tumor stages. The model was trained on the data summarized in Table 2 below using the ground truth of actual metastasis or prostate cancer specific mortality events experienced by the patients in the trials from which the data is extracted. There were 1,133 distant metastasis events and 931 prostate cancer specific mortality events in the dataset used to train the model. Additional information about training dataset is presented in Table 2 below:

Table 2. Characteristics of Training Dataset

Study Name												
Variables	**Total** *N = 10009*[1]	**Canary-PASS** *N = 971*[1]	**RTOG[11]-0126** *N = 1110*[1]	**RTOG-0415** *N = 714*[1]	**RTOG-0521** *N = 351*[1]	**RTOG-9202** *N = 1251*[1]	**RTOG-9408** *N = 1721*[1]	**RTOG-9413** *N = 946*[1]	**RTOG-9902** *N = 335*[1]	**RTOG-9910** *N = 981*[1]	**STAMPEDE** *N = 1589*[1]	**Contemporary Biopsy Cohort A** *N = 40*[1]
Treatment Per Protocol[2]												
AS[3]	971 (9.7%)	971 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (-)
RT[4]-only	2,697 (27%)	0 (0%)	1,110 (100%)	714 (100%)	0 (0%)	0 (0%)	873 (51%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (-)
RT + ST-ADT[5]	2,898 (29%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	619 (49%)	848 (49%)	946 (100%)	0 (0%)	485 (49%)	0 (0%)	0 (-)
RT + IT-ADT[6]	496 (5.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	496 (51%)	0 (0%)	0 (-)
RT + LT-ADT[7]	974 (9.8%)	0 (0%)	0 (0%)	0 (0%)	170 (48%)	632 (51%)	0 (0%)	0 (0%)	172 (51%)	0 (0%)	0 (0%)	0 (-)
RT + LT-ADT + Chemo	344 (3.5%)	0 (0%)	0 (0%)	0 (0%)	181 (52%)	0 (0%)	0 (0%)	0 (0%)	163 (49%)	0 (0%)	0 (0%)	0 (-)
ADT +/- RT	791 (7.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	791 (50%)	0 (-)
ADT + Chemo +/- ZA[8]	237 (2.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	237 (15%)	0 (-)
ADT + Abi[9] +/- Enza[10]	561 (5.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	561 (35%)	0 (-)
Missing	40	0	0	0	0	0	0	0	0	0	0	40
Age at time of biopsy/randomization												
Median (Q1 - Q3)	69 (64 - 73)	63 (58 - 67)	71 (65 - 74)	68 (62 - 73)	66 (59 - 72)	70 (66 - 74)	71 (66 - 74)	70 (65 - 74)	66 (60 - 71)	71 (65 - 74)	68 (63 - 72)	64 (58 - 68)
Min - Max	33 - 91	39 - 81	33 - 87	45 - 84	48 - 83	43 - 88	47 - 91	44 - 87	42 - 81	46 - 88	41 - 86	46 - 74
Race												
African American	1,316 (13%)	68 (7.0%)	115 (10%)	107 (15%)	34 (9.7%)	153 (12%)	334 (19%)	236 (25%)	92 (27%)	166 (17%)	0 (0%)	11 (28%)
White	6,777 (68%)	866 (89%)	960 (86%)	584 (82%)	306 (87%)	1,065 (85%)	1,314 (76%)	653 (69%)	230 (69%)	774 (79%)	0 (0%)	25 (63%)
Other	285 (2.8%)	37 (3.8%)	21 (1.9%)	15 (2.1%)	8 (2.3%)	27 (2.2%)	70 (4.1%)	51 (5.4%)	12 (3.6%)	40 (4.1%)	0 (0%)	4 (10%)
Unknown	1,631 (16%)	0 (0%)	14 (1.3%)	8 (1.1%)	3 (0.9%)	6 (0.5%)	3 (0.2%)	6 (0.6%)	1 (0.3%)	1 (0.1%)	1,589 (100%)	0 (0%)
PSA (ng/mL) at time of biopsy/ randomization												
Median (Q1 - Q3)	10.4 (6.1 - 22.2)	5.0 (3.9 - 6.6)	7.6 (5.4 - 10.6)	5.5 (4.4 - 7.1)	15.7 (7.3 - 37.7)	20.1 (11.0 - 39.7)	8.1 (5.8 - 11.7)	23.4 (12.6 - 36.0)	22.9 (9.5 - 40.7)	10.9 (6.8 - 15.0)	40.0 (15.9 - 80.3)	6.2 (4.7 - 10.9)
Min - Max	0.1 - 2,870.0	0.3 - 19.5	0.1 - 19.9	0.1 - 10.0	0.7 - 145.0	0.1 - 250.0	0.1 - 20.0	2.1 - 97.6	1.8 - 96.4	0.6 - 72.9	0.6 - 2,870.0	2.6 - 61.9
Missing	10	0	0	0	0	0	0	0	0	10	0	0
Tumor Stage												
T1-T2a	5,267 (53%)	964 (99%)	952 (86%)	671 (94%)	117 (33%)	0 (0%)	1,385 (80%)	210 (22%)	126 (38%)	800 (82%)	8 (0.5%)	34 (85%)
T2b-c	1,971 (20%)	7 (0.7%)	158 (14%)	43 (6.0%)	134 (38%)	565 (45%)	336 (20%)	398 (42%)	101 (30%)	123 (13%)	101 (6.4%)	5 (13%)
T3a	442 (4.4%)	0 (0%)	0 (0%)	0 (0%)	45 (13%)	184 (15%)	0 (0%)	138 (15%)	50 (15%)	25 (2.5%)	0 (0%)	0 (0%)
T3b-T4	2,307 (23%)	0 (0%)	0 (0%)	0 (0%)	55 (16%)	502 (40%)	0 (0%)	200 (21%)	58 (17%)	33 (3.4%)	1,458 (93%)	1 (2.5%)
Missing	22	0	0	0	0	0	0	0	0	0	22	0
Gleason Grade Group												
1	3,866 (39%)	894 (92%)	169 (15%)	713 (100%)	0 (0%)	472 (40%)	1,049 (62%)	255 (27%)	0 (0%)	273 (28%)	29 (1.8%)	12 (30%)

2	2,147 (22%)	77 (7.9%)	676 (61%)	0 (0%)	34 (9.7%)	242 (21%)	309 (18%)	254 (27%)	55 (16%)	371 (38%)	118 (7.4%)	11 (28%)
2/3	52 (0.5%)	0 (0%)	1 (<0.1%)	0 (0%)	1 (0.3%)	25 (2.1%)	10 (0.6%)	11 (1.2%)	0 (0%)	4 (0.4%)	0 (0%)	0 (0%)
3	1,188 (12%)	0 (0%)	264 (24%)	0 (0%)	22 (6.3%)	132 (11%)	155 (9.2%)	155 (16%)	56 (17%)	224 (23%)	175 (11%)	5 (13%)
4	1,169 (12%)	0 (0%)	0 (0%)	0 (0%)	110 (31%)	157 (13%)	114 (6.8%)	161 (17%)	115 (34%)	77 (7.8%)	429 (27%)	6 (15%)
5	1,459 (15%)	0 (0%)	0 (0%)	0 (0%)	184 (52%)	141 (12%)	45 (2.7%)	109 (12%)	109 (33%)	32 (3.3%)	833 (53%)	6 (15%)
Missing	128	0	0	1	0	82	39	1	0	0	5	0
NCCN risk group												
Low	2,091 (21%)	828 (85%)	0 (0%)	670 (94%)	0 (0%)	0 (0%)	577 (34%)	0 (0%)	0 (0%)	6 (0.6%)	0 (0%)	10 (25%)
Intermediate	3,381 (34%)	143 (15%)	1,110 (100%)	40 (5.6%)	1 (0.3%)	233 (19%)	946 (56%)	154 (16%)	1 (0.3%)	717 (74%)	19 (1.2%)	17 (43%)
High	4,469 (45%)	0 (0%)	0 (0%)	0 (0%)	350 (100%)	1,001 (81%)	159 (9.5%)	792 (84%)	334 (100%)	250 (26%)	1,570 (99%)	13 (33%)
Missing	68	0	0	4	0	17	39	0	0	8	0	0
Distant Metastasis												
No	8,836 (89%)	966 (99%)	1,017 (92%)	709 (99%)	281 (80%)	982 (78%)	1,580 (92%)	753 (80%)	292 (87%)	933 (95%)	1,323 (83%)	0 (-)
Yes	1,133 (11%)	5 (0.5%)	93 (8.4%)	5 (0.7%)	70 (20%)	269 (22%)	141 (8.2%)	193 (20%)	43 (13%)	48 (4.9%)	266 (17%)	0 (-)
Missing	40	0	0	0	0	0	0	0	0	0	0	40
Cancer-Specific Mortality												
No	8,067 (90%)	0 (-)	1,050 (95%)	711 (100%)	305 (87%)	996 (80%)	1,604 (93%)	776 (82%)	305 (91%)	951 (97%)	1,369 (86%)	0 (-)
Yes	931 (10%)	0 (-)	60 (5.4%)	3 (0.4%)	46 (13%)	255 (20%)	117 (6.8%)	170 (18%)	30 (9.0%)	30 (3.1%)	220 (14%)	0 (-)
Missing	1,011	971	0	0	0	0	0	0	0	0	0	40
Follow-up time of the censored (year)												
Median (Q1 - Q3)	8.7 (6.0 - 11.8)	9.6 (7.1 - 11.8)	13.2 (11.7 - 14.5)	6.0 (5.1 - 6.9)	10.5 (9.5 - 11.6)	17.6 (9.1 - 19.7)	15.1 (7.3 - 17.9)	13.8 (7.2 - 17.5)	10.0 (9.1 - 11.8)	9.3 (8.2 - 10.5)	6.1 (5.1 - 7.5)	-
Min - Max	0.0 - 24.8	0.3 - 24.8	0.0 - 17.7	0.3 - 8.5	0.2 - 12.9	0.4 - 22.0	0.2 - 21.9	0.0 - 20.0	0.4 - 13.3	0.0 - 12.4	1.8 - 11.9	-

[1]n (%). Note that some percentages may not add up to a hundred percent due to rounding; [2]Treatment Per Protocol (e.g., randomization assignment); [3] Active Surveillance; [4] Radiation Therapy; [5] Short Term Androgen Deprivation Therapy; [6] Intermediate Term Androgen Deprivation Therapy; [7] Long Term Androgen Deprivation Therapy; [8] Zoledronic Acid; [9] Abiraterone; [10] Enzalutamide; [11] Radiation Therapy Oncology Group

D. Software and Cybersecurity

ArteraAI Prostate software documentation and software verification and validation testing demonstrate that the device followed all recommendations for basic documentation level as outlined in the FDA guidance document, "*Content of Premarket Submissions for Device Software Functions," issued on June 14, 2023*. A description of the testing protocols, including pass/fail criteria, and report of results was provided for the verification and validation activities and all testing results met design specifications and passed the acceptance criteria.

ArteraAI Prostate cybersecurity documentation demonstrated that the device met the cybersecurity requirements as outlined in Section 524B of Federal Food, Drug, and Cosmetic Act (FD&C Act). This includes a threat model, software bill of materials, data security training, validation and mitigation of cybersecurity risks, cyber risk management, labeling, cyber testing, and post market cyber vulnerabilities and other information for safeguarding the algorithms.

V Standards/Guidance Documents Referenced:

1. Guidance for the Content of Premarket Submissions for Device Software Functions; June 2023
2. CLSI document EP12-Ed3: Evaluation of Qualitative, Binary Output Examination Performance; March 2023
3. Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions; September 2023
4. The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]; July 2014
5. Guidance for Industry and FDA Staff: De Novo Classification Process (Evaluation of Automatic Class III Designation); October 2021
6. Acceptance of Clinical Data to Support Medical Device Applications and Submissions Frequently Asked Questions; February 2018
7. Guidance for Industry and Food and Drug Administration Staff - Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications; August 2019
8. Guidance for Off-the-Shelf Software Use in Medical Devices; August 2023
9. ISO 14971 Third Edition 2019-12 Medical devices - Application of risk management to medical devices
10. IEC 62304 Edition 1.1 2015-06 (2015). Medical device software – Software life cycle processes
11. IEC 62366-1 Edition 1.1 2020-06 CONSOLIDATED VERSION – Medical devices – Part 1: Application of usability engineering to medical devices

VI Performance Characteristics:

A. Analytical Performance:

The precision of ArteraAI device was evaluated in a between-site reproducibility study which was performed at three laboratory sites in the United States. At each site, slides were scanned by a single operator on a Philips Ultra Fast scanner at 40x objective, with one run per day and five replicates per run, over five non-consecutive days (total number=15). Fifty-two samples (including 6 borderline samples based on ArteraAI Prostate raw score cut-offs) were included in the between-site reproducibility study and these samples were selected from patients with an age at biopsy from 55 years and above, Gleason score 6 to 10, clinical stage T1 to T3, and spanning the low-, intermediate-, and high-risk categories of the device output. The sample characteristics are provided in Table 3 below.

Table 3. Characteristics of Samples Used in Analytical Studies

Characteristic	N = 52
Age (year), Median, (Min, Max)	66, (55, 86)
PSA (ng/mL), Median, (Min, Max)	6.95, (1.14, 577.42)
Tumor Stage, n (%)	
T1	35.0 (67.3%)
T2	15.0 (28.8%)
T3	2.0 (3.8%)
Gleason Grade Group, n (%)	
GG 1	14.0 (26.9%)
GG 2	17.0 (32.7%)
GG 3	11.0 (21.2%)
GG 4	5.0 (9.6%)
GG 5	5.0 (9.6%)
NCCN Risk Category, n (%)	
Very Low/Low	11.0 (21.2%)
Intermediate	31.0 (59.6%)
High/Very High	10.0 (19.2%)
ArteraAI Risk Group (Case-Level Mode) n (%)	
Low Risk	17.0 (32.7%)
Intermediate Risk	20.0 (38.5%)
High Risk	15.0 (28.8%)
Borderline Group (Case-Level Mean Within Borderline Threshold), n (%)	
Borderline	6.0 (11.5%)
Non-Borderline	46.0 (88.5%)
n (%). Note that some percentages may not add up to a hundred percent due to rounding	

Summary of Analytical Validation Study Results:

a. Analysis of numeric values of the raw score was performed according to CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures, 3rd Edition. Within-laboratory, between-site and reproducibility were calculated; in addition, a qualitative analysis (percent of each ArteraAI categories among 15 replicates) was performed and results of these analyses are presented in Table 4 below.

b. Analysis of 10-year DM values for cases with Low- and Intermediate- risk categories was also performed according to the CLSI EP05-A3. Within-laboratory, between-site and reproducibility were calculated; in addition, a qualitative analysis (percent of each ArteraAI categories among 15 replicates) was performed and results of these analyses are presented in Table 5.

c. For ArteraAI raw scores, the %CV for the within-site precision (the same scanner on different days) ranged from 0.1% to 2.8%; the %CV for the between-site precision ranged from 0.0% to 6.0% and %CV for reproducibility ranged from 0.3% to 6.1%.

d. For ArteraAI DM scores, the %CV for the within-site precision (the same scanner on different days) ranged from 0.5% to 5.7%; the %CV for the between-site precision ranged from 0.0% to 12.3% and %CV for reproducibility ranged from 1.0% to 12.3%.

Table 4. Within-Site Precision and Reproducibility of ArteraAI Raw Score

Sample	Mean Raw score	ArteraAI Risk Group (Case-Level Mode)	Borderline Cases	Within-Site		Between-Site		Reproducibility (Total)		Percent Category Agreement Results based on Case-Level Category Call Mode			Percent Category Agreement Results		
				SD	%CV	SD	%CV	SD	%CV	Site 1	Site 2	Site 3	Percent Low	Percent Intermediate	Percent High
1	0.185	Low	Non-Borderline	0.001806	1.0	0.004039	2.2	0.004425	2.4	100.0%	100.0%	100.0%	100%	0%	0%
2	0.205	Low	Non-Borderline	0.001309	0.6	0.002012	1.0	0.002400	1.2	100.0%	100.0%	100.0%	100%	0%	0%
3	0.212	Low	Non-Borderline	0.001271	0.6	0.005407	2.6	0.005555	2.6	100.0%	100.0%	100.0%	100%	0%	0%
4	0.214	Low	Non-Borderline	0.000956	0.4	0.007615	3.6	0.007675	3.6	100.0%	100.0%	100.0%	100%	0%	0%
5	0.219	Low	Non-Borderline	0.001893	0.9	0.007039	3.2	0.007289	3.3	100.0%	100.0%	100.0%	100%	0%	0%
6	0.226	Low	Non-Borderline	0.004294	1.9	0.007521	3.3	0.008661	3.8	100.0%	100.0%	100.0%	100%	0%	0%
7	0.226	Low	Non-Borderline	0.000857	0.4	0.001573	0.7	0.001791	0.8	100.0%	100.0%	100.0%	100%	0%	0%
8	0.229	Low	Non-Borderline	0.002214	1.0	0.000000	0.0	0.002214	1.0	100.0%	100.0%	100.0%	100%	0%	0%
9	0.230	Low	Non-Borderline	0.002779	1.2	0.005070	2.2	0.005781	2.5	100.0%	100.0%	100.0%	100%	0%	0%
10	0.238	Low	Non-Borderline	0.001154	0.5	0.002927	1.2	0.003146	1.3	100.0%	100.0%	100.0%	100%	0%	0%
11	0.242	Low	Non-Borderline	0.001742	0.7	0.000497	0.2	0.001812	0.7	100.0%	100.0%	100.0%	100%	0%	0%
12	0.265	Low	Non-Borderline	0.001443	0.5	0.001743	0.7	0.002263	0.9	100.0%	100.0%	100.0%	100%	0%	0%
13	0.282	Low	Non-Borderline	0.002107	0.7	0.003652	1.3	0.004216	1.5	100.0%	100.0%	100.0%	100%	0%	0%
14	0.289	Low	Non-Borderline	0.002227	0.8	0.005834	2.0	0.006244	2.2	100.0%	100.0%	100.0%	100%	0%	0%
15	0.290	Low	Non-Borderline	0.003115	1.1	0.003817	1.3	0.004927	1.7	100.0%	100.0%	100.0%	100%	0%	0%
16	0.303	Low	Borderline	0.001772	0.6	0.005988	2.0	0.006245	2.1	100.0%	100.0%	20.0%	73%	27%	0%
17	0.306	Low	Borderline	0.001559	0.5	0.003432	1.1	0.003769	1.2	20.0%	60.0%	100.0%	60%	40%	0%
18	0.312	Intermediate	Borderline	0.008688	2.8	0.001461	0.5	0.008810	2.8	80.0%	80.0%	100.0%	13%	87%	0%
19	0.314	Intermediate	Borderline	0.001071	0.3	0.009940	3.2	0.009998	3.2	100.0%	100.0%	0.0%	33%	67%	0%
20	0.325	Intermediate	Non-Borderline	0.002732	0.8	0.000000	0.0	0.002732	0.8	100.0%	100.0%	100.0%	0%	100%	0%
21	0.328	Intermediate	Non-Borderline	0.001701	0.5	0.019817	6.0	0.019890	6.1	100.0%	100.0%	100.0%	0%	100%	0%
22	0.349	Intermediate	Non-Borderline	0.003322	1.0	0.013573	3.9	0.013974	4.0	100.0%	100.0%	100.0%	0%	100%	0%
23	0.350	Intermediate	Non-Borderline	0.002170	0.6	0.001723	0.5	0.002771	0.8	100.0%	100.0%	100.0%	0%	100%	0%
24	0.352	Intermediate	Non-Borderline	0.004187	1.2	0.003820	1.1	0.005668	1.6	100.0%	100.0%	100.0%	0%	100%	0%
25	0.355	Intermediate	Non-Borderline	0.001203	0.3	0.005651	1.6	0.005777	1.6	100.0%	100.0%	100.0%	0%	100%	0%
26	0.371	Intermediate	Non-Borderline	0.001948	0.5	0.001776	0.5	0.002636	0.7	100.0%	100.0%	100.0%	0%	100%	0%
27	0.371	Intermediate	Non-Borderline	0.001099	0.3	0.002040	0.5	0.002317	0.6	100.0%	100.0%	100.0%	0%	100%	0%
28	0.384	Intermediate	Non-Borderline	0.001453	0.4	0.005392	1.4	0.005584	1.5	100.0%	100.0%	100.0%	0%	100%	0%

Sample	Mean Raw score	ArteraAI Risk Group (Case-Level Mode)	Borderline Cases	Within-Site		Between-Site		Reproducibility (Total)		Percent Category Agreement Results based on Case-Level Category Call Mode			Percent Category Agreement Results		
				SD	%CV	SD	%CV	SD	%CV	Site 1	Site 2	Site 3	Percent Low	Percent Intermediate	Percent High
29	0.390	Intermediate	Non-Borderline	0.005359	1.4	0.004235	1.1	0.006831	1.8	100.0%	100.0%	100.0%	0%	100%	0%
30	0.397	Intermediate	Non-Borderline	0.001491	0.4	0.005010	1.3	0.005227	1.3	100.0%	100.0%	100.0%	0%	100%	0%
31	0.400	Intermediate	Non-Borderline	0.001195	0.3	0.003167	0.8	0.003385	0.8	100.0%	100.0%	100.0%	0%	100%	0%
32	0.407	Intermediate	Non-Borderline	0.001038	0.3	0.001365	0.3	0.001715	0.4	100.0%	100.0%	100.0%	0%	100%	0%
33	0.413	Intermediate	Non-Borderline	0.002663	0.6	0.003802	0.9	0.004642	1.1	100.0%	100.0%	100.0%	0%	100%	0%
34	0.420	Intermediate	Non-Borderline	0.002113	0.5	0.014643	3.5	0.014795	3.5	100.0%	100.0%	40.0%	0%	80%	20%
35	0.426	Intermediate	Non-Borderline	0.004043	1.0	0.000000	0.0	0.004043	1.0	100.0%	100.0%	100.0%	0%	100%	0%
36	0.436	Intermediate	Borderline	0.002847	0.7	0.014866	3.4	0.015136	3.5	80.0%	100.0%	0.0%	0%	60%	40%
37	0.438	Intermediate	Borderline	0.002632	0.6	0.006176	1.4	0.006714	1.5	100.0%	80.0%	0.0%	0%	60%	40%
38	0.445	High	Non-Borderline	0.001581	0.4	0.007081	1.6	0.007255	1.6	100.0%	100.0%	100.0%	0%	0%	100%
39	0.448	High	Non-Borderline	0.004839	1.1	0.003849	0.9	0.006183	1.4	100.0%	100.0%	100.0%	0%	0%	100%
40	0.461	High	Non-Borderline	0.001674	0.4	0.014430	3.1	0.014527	3.1	100.0%	100.0%	100.0%	0%	0%	100%
41	0.472	High	Non-Borderline	0.001756	0.4	0.004479	0.9	0.004811	1.0	100.0%	100.0%	100.0%	0%	0%	100%
42	0.487	High	Non-Borderline	0.004797	1.0	0.007514	1.5	0.008915	1.8	100.0%	100.0%	100.0%	0%	0%	100%
43	0.507	High	Non-Borderline	0.001724	0.3	0.001841	0.4	0.002522	0.5	100.0%	100.0%	100.0%	0%	0%	100%
44	0.513	High	Non-Borderline	0.002262	0.4	0.005683	1.1	0.006116	1.2	100.0%	100.0%	100.0%	0%	0%	100%
45	0.548	High	Non-Borderline	0.004224	0.8	0.004849	0.9	0.006431	1.2	100.0%	100.0%	100.0%	0%	0%	100%
46	0.571	High	Non-Borderline	0.002129	0.4	0.003163	0.6	0.003813	0.7	100.0%	100.0%	100.0%	0%	0%	100%
47	0.587	High	Non-Borderline	0.000962	0.2	0.004616	0.8	0.004715	0.8	100.0%	100.0%	100.0%	0%	0%	100%
48	0.601	High	Non-Borderline	0.001474	0.2	0.002438	0.4	0.002849	0.5	100.0%	100.0%	100.0%	0%	0%	100%
49	0.619	High	Non-Borderline	0.000929	0.2	0.003225	0.5	0.003356	0.5	100.0%	100.0%	100.0%	0%	0%	100%
50	0.707	High	Non-Borderline	0.001207	0.2	0.004154	0.6	0.004326	0.6	100.0%	100.0%	100.0%	0%	0%	100%
51	0.717	High	Non-Borderline	0.000674	0.1	0.001893	0.3	0.002009	0.3	100.0%	100.0%	100.0%	0%	0%	100%
52	0.739	High	Non-Borderline	0.005590	0.8	0.006197	0.8	0.008345	1.1	100.0%	100.0%	100.0%	0%	0%	100%
n: 52															

Table 5. Within-Site Precision and Reproducibility of ArteraAI Prostate DM Risk

Sample	Mean	ArteraAI Risk Group (Case-Level Mode)	Borderline Cases	Within-Site		Between-Site		Reproducibility (Total)		Percent Category Agreement Results based on Case-Level Category Call Mode			Percent Category Agreement Results		
				SD	%CV	SD	%CV	SD	%CV	Site 1	Site 2	Site 3	Percent Low	Percent Intermediate	Percent High
1	0.022	Low	Non-Borderline	0.000238	1.1	0.000530	2.5	0.000581	2.7	100.0%	100.0%	100.0%	100%	0%	0%
2	0.024	Low	Non-Borderline	0.000193	0.8	0.000299	1.2	0.000356	1.5	100.0%	100.0%	100.0%	100%	0%	0%
3	0.025	Low	Non-Borderline	0.000199	0.8	0.000847	3.3	0.000870	3.4	100.0%	100.0%	100.0%	100%	0%	0%
4	0.026	Low	Non-Borderline	0.000153	0.6	0.001217	4.7	0.001226	4.7	100.0%	100.0%	100.0%	100%	0%	0%
5	0.027	Low	Non-Borderline	0.000319	1.2	0.001155	4.3	0.001198	4.5	100.0%	100.0%	100.0%	100%	0%	0%
6	0.028	Low	Non-Borderline	0.000783	2.8	0.001298	4.7	0.001516	5.5	100.0%	100.0%	100.0%	100%	0%	0%
7	0.028	Low	Non-Borderline	0.000144	0.5	0.000266	1.0	0.000303	1.1	100.0%	100.0%	100.0%	100%	0%	0%
8	0.028	Low	Non-Borderline	0.000381	1.4	0.000000	0.0	0.000381	1.4	100.0%	100.0%	100.0%	100%	0%	0%
9	0.028	Low	Non-Borderline	0.000478	1.7	0.000874	3.1	0.000996	3.5	100.0%	100.0%	100.0%	100%	0%	0%
10	0.030	Low	Non-Borderline	0.000206	0.7	0.000533	1.8	0.000571	1.9	100.0%	100.0%	100.0%	100%	0%	0%
11	0.031	Low	Non-Borderline	0.000324	1.1	0.000092	0.3	0.000337	1.1	100.0%	100.0%	100.0%	100%	0%	0%
12	0.035	Low	Non-Borderline	0.000308	0.9	0.000371	1.1	0.000482	1.4	100.0%	100.0%	100.0%	100%	0%	0%
13	0.039	Low	Non-Borderline	0.000495	1.3	0.000862	2.2	0.000994	2.6	100.0%	100.0%	100.0%	100%	0%	0%
14	0.041	Low	Non-Borderline	0.000561	1.4	0.001442	3.5	0.001547	3.8	100.0%	100.0%	100.0%	100%	0%	0%
15	0.041	Low	Non-Borderline	0.000797	1.9	0.000960	2.3	0.001247	3.0	100.0%	100.0%	100.0%	100%	0%	0%
16	0.044	Low	Borderline	0.000476	1.1	0.001619	3.7	0.001688	3.8	100.0%	100.0%	20.0%	73%	27%	0%
17	0.045	Low	Borderline	0.000427	0.9	0.000929	2.1	0.001023	2.3	20.0%	60.0%	100.0%	60%	40%	0%
18	0.047	Intermediate	Borderline	0.000314	0.7	0.002804	5.9	0.002822	5.9	100.0%	100.0%	0.0%	33%	67%	0%
19	0.047	Intermediate	Borderline	0.002657	5.7	0.000407	0.9	0.002688	5.8	80.0%	80.0%	100.0%	13%	87%	0%
20	0.051	Intermediate	Non-Borderline	0.000835	1.7	0.000000	0.0	0.000835	1.7	100.0%	100.0%	100.0%	0%	100%	0%
21	0.052	Intermediate	Non-Borderline	0.000520	1.0	0.006351	12.3	0.006372	12.3	100.0%	100.0%	100.0%	0%	100%	0%
22	0.059	Intermediate	Non-Borderline	0.001271	2.2	0.004875	8.3	0.005038	8.6	100.0%	100.0%	100.0%	0%	100%	0%
23	0.059	Intermediate	Non-Borderline	0.001542	2.6	0.001350	2.3	0.002050	3.5	100.0%	100.0%	100.0%	0%	100%	0%
24	0.059	Intermediate	Non-Borderline	0.000765	1.3	0.000608	1.0	0.000977	1.7	100.0%	100.0%	100.0%	0%	100%	0%
25	0.061	Intermediate	Non-Borderline	0.000428	0.7	0.002067	3.4	0.002111	3.5	100.0%	100.0%	100.0%	0%	100%	0%
26	0.066	Intermediate	Non-Borderline	0.000774	1.2	0.000702	1.1	0.001045	1.6	100.0%	100.0%	100.0%	0%	100%	0%
27	0.067	Intermediate	Non-Borderline	0.000435	0.7	0.000812	1.2	0.000921	1.4	100.0%	100.0%	100.0%	0%	100%	0%
28	0.072	Intermediate	Non-Borderline	0.000631	0.9	0.002338	3.2	0.002422	3.4	100.0%	100.0%	100.0%	0%	100%	0%
29	0.074	Intermediate	Non-Borderline	0.002295	3.1	0.001834	2.5	0.002938	3.9	100.0%	100.0%	100.0%	0%	100%	0%
30	0.078	Intermediate	Non-Borderline	0.000682	0.9	0.002326	3.0	0.002424	3.1	100.0%	100.0%	100.0%	0%	100%	0%
31	0.079	Intermediate	Non-Borderline	0.000565	0.7	0.001490	1.9	0.001594	2.0	100.0%	100.0%	100.0%	0%	100%	0%

Sample	Mean	ArteraAI Risk Group (Case-Level Mode)	Borderline Cases	Within-Site		Between-Site		Reproducibility (Total)		Percent Category Agreement Results based on Case-Level Category Call Mode			Percent Category Agreement Results		
				SD	%CV	SD	%CV	SD	%CV	Site 1	Site 2	Site 3	Percent Low	Percent Intermediate	Percent High
32	0.082	Intermediate	Non-Borderline	0.000506	0.6	0.000665	0.8	0.000836	1.0	100.0%	100.0%	100.0%	0%	100%	0%
33	0.085	Intermediate	Non-Borderline	0.001342	1.6	0.001908	2.2	0.002332	2.7	100.0%	100.0%	100.0%	0%	100%	0%
34	0.089	Intermediate	Non-Borderline	0.001160	1.3	0.007888	8.8	0.007972	8.9	100.0%	100.0%	40.0%	0%	80%	20%
35	0.092	Intermediate	Non-Borderline	0.002180	2.4	0.000000	0.0	0.002180	2.4	100.0%	100.0%	100.0%	0%	100%	0%
36	0.098	Intermediate	Borderline	0.001628	1.7	0.008692	8.9	0.008843	9.0	80.0%	100.0%	0.0%	0%	60%	40%
37	0.099	Intermediate	Borderline	0.001563	1.6	0.003636	3.7	0.003958	4.0	100.0%	80.0%	0.0%	0%	60%	40%
n: 37															

B Clinical Performance:

The clinical performance of the ArteraAI Prostate device was evaluated in a retrospective clinical study which included a total of 886 patients across three sites in the US. The dataset for pivotal clinical performance study included patients with non-metastatic prostate cancer diagnosed since 2005 without clinically or pathologically defined metastases. Patients across 3 US sites were considered eligible if age at date of biopsy was 55 years of age and older with clinical T-stage T1-T4 (T1a, T1b, T1c, T1, T2a, T2b, T2c, T2, T3a, T3b, T3c, T4a, T4b, T4c, T4), baseline median PSA value closest to the biopsy were 6.2 ng/mL, and Gleason score at diagnosis was 6-10. The intended patient should also have been a candidate for curative intent management (surgery, radiation therapy with or without systemic therapy), or active surveillance. Patients were required to have non-metastatic prostate cancer and at least one H&E slide containing at least one FFPE biopsy core with the highest Gleason grade tumor as diagnosed by the pathologist. The slides were scanned to a digital image format using the Philips Ultra Fast Scanner. Patients with prior or concurrent malignancy (except non-melanoma skin cancer) within the 5 years prior to prostate cancer diagnosis, recurring cancer, metastatic disease at diagnosis or patients who received only palliative care were excluded from the study resulting in pivotal clinical performance cohort of N=886.

The summary of patient characteristics for the pivotal clinical performance study is presented in Table 6 below.

Table 6. Summary of Clinical Validation Patient Cohort Characteristics

Variables	Overall N = 886[1]
Sites, n(%)	
Site 1	290 (33%)
Site 2	444 (50%)
Site 3	152 (17%)
Treatment Per Protocol, n(%)	
Active Surveillance	314 (36%)
Radiation Therapy (With or without Androgen Deprivation Therapy)	203 (23%)
Radical Prostatectomy	354 (41%)
Missing	15
Age at time of biopsy	
Median (Q1 - Q3)	65 (61 - 70)
Min - Max	55 - 98
Race, n(%)	
Black	72 (8.1%)
White	675 (76%)
Other	133 (15%)
Unknown	6 (0.7%)
PSA (ng/mL) at time of biopsy	
Median (Q1 - Q3)	6.2 (4.6 - 9.6)
Clinical Tumor Stage, n(%)	
T1a	3 (0.3%)
T1b	1 (0.1%)
T1c	579 (65%)
T2	2 (0.2%)
T2a	178 (20%)
T2b	48 (5.4%)
T2c	46 (5.2%)
T3a	20 (2.3%)
T3b	6 (0.7%)
T4	3 (0.3%)

Variables	Overall N = 886[1]
Gleason Grade Group at time of biopsy, n(%)	
1	372 (42%)
2	220 (25%)
3	132 (15%)
4	97 (11%)
5	64 (7.2%)
Missing	1
NCCN risk group (3-level), n(%)	
Low	313 (35%)
Intermediate	358 (40%)
High	206 (23%)
N1-3[2]	7 (0.8%)
Missing	2
Follow-up time of the censored (year)	
Median (Q1 - Q3)	8.2 (6.2 - 11.2)
Min - Max	0.1 - 18.7

[1]n (%). Note that some percentages may not add up to a 100% due to rounding
[2]Clinically node positive patients, not applicable for NCCN risk grouping

Summary of Clinical Validation Results:

a. 10-Year Risk of DM for ArteraAI Prostate Risk Categories (High, Intermediate, Low)

The prognostic ability of the ArteraAI Prostate was evaluated for 10-year risk of DM.

The estimates of 10-year risks of DM for ArteraAI Prostate Risk categories along with two-sided 95%CI are presented in Table 7 and Figure 2 below.

The results of the pivotal clinical performance study support that:

i. 10-year risk of DM for ArteraAI Prostate Risk category High (28.1%) is statistically significantly higher than the overall risk (8.1%) and this difference (20.0%) is clinically significant.

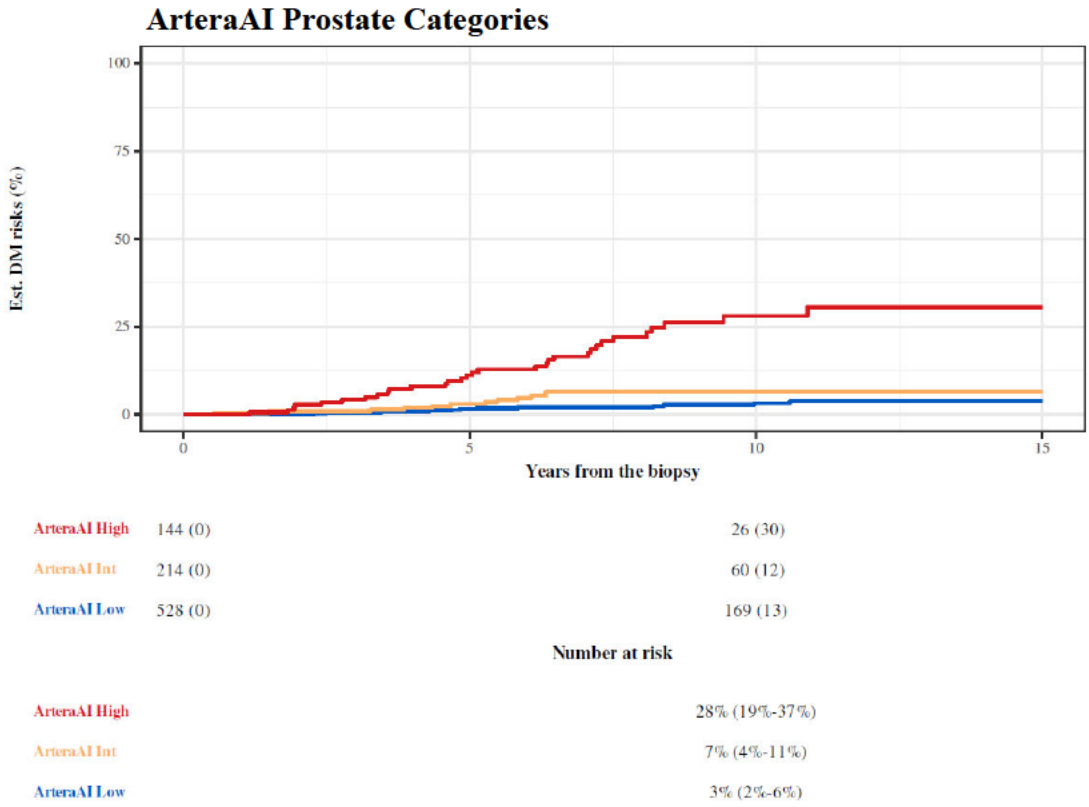
ii. 10-year risk of DM for ArteraAI Prostate Risk category Low (3.3%), is statistically significantly lower than the overall risk (8.1%) and this difference (4.8%) is clinically significant.

Table 7. 10-Year Risks of DM for Artera AI Prostate Risk Categories

ArteraAI Prostate Risk Category	Total Number	Number of DM for 10 years	Estimated 10-year Risk of DM (95% CI) *	Percentage of Patients with the Risk Category (Total/886)
High	144	30	28.1% (19.4%-37.5%)	16.3%
Intermediate	214	12	6.6% (3.6%-10.8%)	24.2%
Low	528	13	3.3% (1.8%-5.6%)	59.6%
Total	886	55	Estimated overall risk (95% CI): 8.1% (6.1%-10.4%)	

* The estimated 10-year risk of DM and 95% CI were calculated by Kaplan- Meier survival analysis.

Figure 2. Kaplan-Meier curves for 10-Year Risk of DM for ArteraAI Prostate Risk Categories (High, Intermediate, Low)



b. 10-Year Risk of PCSM for ArteraAI Prostate Risk Categories (High, Intermediate, Low)

The prognostic ability of the ArteraAI Prostate was evaluated for 10-year risk of PCSM. Estimates of 10-year risks of PCSM for ArteraAI Prostate Risk categories along with two-sided 95%CI are presented in Table 8 and Figure 3.

The results of the pivotal clinical performance study support that:

i. 10-year risk of PCSM for ArteraAI Prostate Risk category High (10.2%), is statistically significantly higher than the overall risk (2.3%) and this difference (7.9%) is clinically significant.

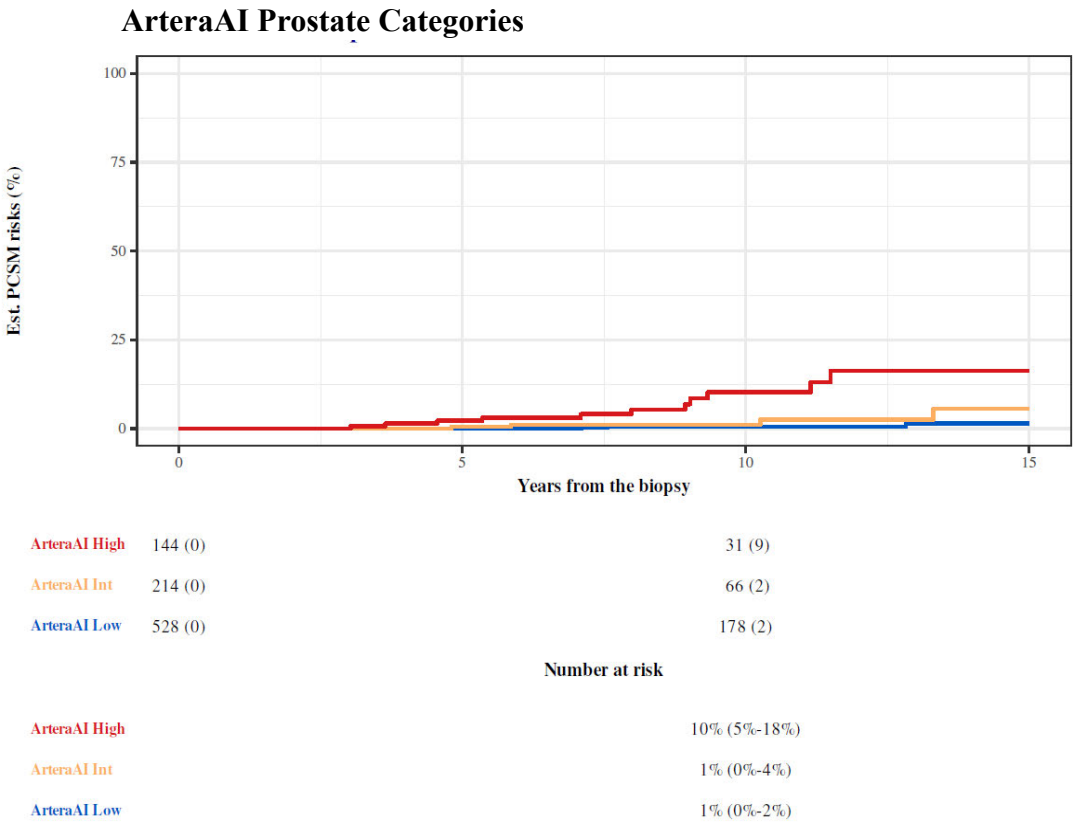
ii. 10-year risk of PCSM for ArteraAI Prostate Risk category Low (0.6%), is statistically significantly lower than the overall risk (2.3%) and this difference (1.7%) is clinically significant.

Table 8. 10-year Risk for PCSM for ArteraAI Prostate Risk Categories

ArteraAI Prostate Risk Category	Total Number	Number of PCSM for 10 years	Estimated 10-year Risk of PCSM (95% CI) *	Percentage of Patients with the Risk Category (Total/886)
High	144	9	10.2% (4.7% - 18.2%)	16.3%
Intermediate	214	2	1.1% (0.2% - 3.7%)	24.2%
Low	528	2	0.6% (0.1% - 2.0%)	59.6%
Total	886	13	Estimated overall risk (95% CI): 2.3% (1.2% - 3.8%))	

* The estimated 10-year risk of DM and 95% CI were calculated by Kaplan- Meier survival analysis.

Figure 3. Kaplan-Meier curves for 10-Year Risk of PCSM for ArteraAI Prostate Risk Categories (High, Intermediate, Low)



c. Subgroup Analysis for 10-Year Risk of DM for ArteraAI Prostate Risk Categories (Low, Intermediate, High)

i. **African American Vs Non-African American**

This subgroup analysis shows that the ArteraAI Prostate risk categories for 10-year risk of distant metastasis outputs are validated between African American and Non-African American patients. A higher 10-year DM risk estimates for African American patients vs non-African American patients for ArteraAI categories High (35.6% vs 27.4%) and Low (9.0% vs 2.9%,) and overall risk (13.5% vs 7.7%) was observed (Table 9). The number of patients from African American patient group was limited (72) and this should be taken in consideration when using the risk estimates provided by ArteraAI Prostate for African American patients.

Table 9. 10-year Risk of DM for African American Patients

African American Patients (N=72)				
ArteraAI Prostate Risk Category	**Total Number**	**Number of DM for 10 Years**	**Estimated 10-year Risk of DM, (95%CI)**	**Percentage of Patients with the Risk Category**
High	10	2	35.6% (1.6%-77.2%)	13.9%
Intermediate	26	2	8.7% (1.4%-24.8%)	36.1%
Low	36	2	9.0% (1.3%-26.3%)	50.0%
Total	72	6	Estimated overall 10-year DM risk, 95%CI: 13.5% (5.1%-26.1%)	

Table 10. 10-year risk for DM for Non-African American Patients

Non-African American Patients (N=814)				
ArteraAI Prostate Risk Category	**Total Number**	**Number of DM for 10 years**	**Estimated 10-year Risk of DM, (95%CI)**	**Percentage of Patients with the Risk Category**
High	134	28	27.4% (18.6%-36.9%)	16.5%
Intermediate	188	10	6.3% (3.2%-10.8%)	23.1%
Low	492	11	2.9% (1.5%-5.2%)	60.4%
Total	814	49	Estimated overall 10-year DM risk, 95%CI: 7.7% (5.7%-10.0%)	

d. Different Treatment Groups

This subgroup analysis shows that the ArteraAI Prostate risk categories for 10-year risk of distant metastasis outputs are validated across patients treated with all different treatment regimens related to nonmetastatic prostate cancer (Table 11). This subgroup analysis stratified by different types of treatment [Active surveillance (n=314), Radiation therapy (n=203) and radical prostatectomy (n=354)] was performed and ArteraAI Prostate risk estimates were acceptable for each treatment group.

Table 11. 10-year risk of DM for patients with different treatments

Treatment Subgroup (N=871*) (all patients with known treatment types)	ArteraAI Prostate Risk Category (N)	Number of DM for 10 Years	Estimated 10-year Risk of DM (95% CI)	Percentage of Patients with the Risk Category (N=871)
Active Surveillance (N=314)	High (N=24)	5	23.1% (8.0%-42.8%)	2.8%
	Intermediate (N=56)	1	2.1% (0.2%-9.9%)	6.4%
	Low (N=234)	3	2.4% (0.6%-6.7%)	26.9%
Radiation Therapy (N=203)	High (N=64)	16	33.4% (19.6%-47.8%)	7.3%
	Intermediate (N=47)	5	13.6% (4.8%-26.8%)	5.4%
	Low (N=92)	3	3.5% (0.9%-9.0%)	10.6%
Radical Prostatectomy (N=354)	High (N=53)	8	22.6% (9.8%-38.6%)	6.1%
	Intermediate (N=107)	6	6.3% (2.6%-12.6%)	12.3%
	Low (N=194)	6	3.8% (1.5%-7.8%)	22.3%

* For 15 out 886 patients, treatment type information was not available.

e. Additional study: Samples with more than one highest Gleason Grade slides

In addition, a study was conducted for cases with multiple slides containing the highest Gleason grade, 15 cases including 14 cases with 2 slides and 1 case with 3 slides which had the same highest Gleason grade. One out of 15 cases (6.7%) had different ArteraAI Prostate risk categories. In real-life settings, all slides with same highest Gleason grade should be analyzed by the ArteraAI Prostate device and the highest risk category is provided in the patient ArteraAI report.

VII Pre-Determined Change Control Plan

The ArteraAI Prostate includes a pre-determined change control plan (PCCP) approved by the US Food and Drug Administration (FDA). The PCCP provides an overview of the planned modifications which is to add additional FDA cleared WSI scanners as intended use components. As outlined in the PCCP, each modification is designed to address specific differences in device input, ensuring consistent performance and prognostic accuracy. Verification and validation testing will ensure that software updates made to add interoperability with additional FDA cleared scanners will not have an impact on existing interoperable scanners or other functionality. The verification/validation process for each additional scanner is same as the validation process used to show interoperability with the Philips Ultra Fast Scanner that is authorized as part of this De Novo submission.

Specific validation study protocols and acceptance criteria are also detailed in the PCCP to ensure that device maintains the following performance characteristics for the stated modification:

- Addition of additional FDA cleared whole slide image (WSI) scanners as intended use components (Interoperability to an additional WSI scanner)

Per ArteraAI's change control procedure, a change request for the following changes will be created:

i. Update the User Interface to include an additional interoperable scanner in the file upload workflow.
ii. Update the Back End to verify image metadata from files from the new interoperable scanner.
iii. If necessary: Update the Image Converter component to convert compatible files from the new scanner to the expected format for the AI Engine.

Upon successful validation, labeling will be updated in accordance with the authorized PCCP to provide users with current information regarding the device's interoperable scanner.

VIII Proposed Labeling:

The labeling supports the decision to grant the De Novo request for this device.

IX Identified Risks and Mitigations:

Risks to Health	Mitigation Measures
Risk of false positive, false negative, or failure to provide a result.	Certain design verification and validation activities, including certain analytical and clinical studies. Certain labeling information, including certain performance information and limitations.
Incorrect interpretation of test results by the user.	Certain design verification and validation activities. Certain labeling information, including certain performance information and limitations.

X Benefit/Risk Assessment:

A Summary of the Assessment of Benefit:

ArteraAI Prostate device provides 10-year categorical risk (High, Intermediate, Low) for DM and PCSM. The device also provides a 10-year individual risk estimate of DM for Low and Intermediate risk groups. These risk estimates in the IU population are intended to help physicians make more informed treatment decisions. The device may help in reducing under or over treatment of patients by estimating the risk of DM.

B Summary of the Assessment of Risk:

The probable risks associated with the use of this device are mainly due to erroneous results and incorrect use and interpretation of test results by the healthcare providers. Incorrect test results may be due the prognostic ArteraAI Prostate 10-year categorical risk (High, Intermediate, Low) for DM and PCSM being reported as higher or lower than true risk and the individual risk estimate of DM for Low and Intermediate risk groups being reported as higher or lower than true risk. In both scenarios above, there is probable risk of mismanagement of patient care in accordance with professional guidelines, based on false test results from this test, or incorrect interpretation of test results.

C Patient Perspectives:

This submission did not include specific information on patient perspectives for this device.

D Summary of the Assessment of Benefit-Risk:

The probable benefit of this device was demonstrated by analytical and clinical validation studies (refer to Section VI Performance Characteristics for details). The clinical performance of ArteraAI device was evaluated in a clinical study which included a total of 886 patients across three sites in the US. The pivotal clinical performance study showed that the 10-year risk of DM for ArteraAI Prostate risk category High (28.1%) is statistically significantly higher than the overall risk (8.1%) and this difference (20.0%) is clinically significant. The 10-year risk of DM for ArteraAI Prostate category Low (3.3%) is statistically significantly lower than the overall risk (8.1%) and this difference (4.8%) is clinically significant.

False test results from this test, or incorrect interpretation of test results, could result in improper medical management of patients. The probable risks associated with false test results includes prognostic ArteraAI Prostate 10-year categorical risk (High, intermediate, Low) for DM and PCSM and prognostic ArteraAI 10-year individual risk estimate of DM for Low and Intermediate risk groups being reported as higher or lower than the true risk. These risks are mitigated by adequate analytical and clinical performance of the device. The probable risks associated with incorrect interpretation of test results are mitigated by inclusion of adequate instructions in the labeling on proper use of the device within the clinical workflow. Further, the

test results are unlikely to be the only factor considered while making clinical decisions. These results may support risk-based decisions within recommended guidelines.

While general controls are insufficient to ensure the safety and effectiveness of the device, in light of the mitigations provided by the special controls, the probable benefits outweigh the probable risks for the use of the ArteraAI Prostate device.

XI Conclusion:

The De Novo request is granted, and the device is classified under the following and subject to the special controls identified in the letter granting the De Novo request:

Product Code(s): SFH
Device Type: Software algorithm device analyzing digital images for cancer prognosis
Class: II
Regulation: 21 CFR 864.3755