SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Free Prostate Specific Antigen (free PSA)

Device Trade Name: Atellica IM free PSA II (fPSAII)

Device Procode: MTG

Applicant's Name and Address:
Siemens Healthcare Diagnostics, Inc.
511 Benedict Ave
Tarrytown, NY 10591

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P250026

Date of FDA Notice of Approval: May 11, 2026

II. INDICATIONS FOR USE

The Atellica IM free PSA II (fPSAII) assay is for in vitro diagnostic use in the quantitative measurement of free prostate-specific antigen (fPSA) in human serum and plasma (lithium heparin and EDTA) using the Atellica IM Analyzer. The Atellica IM fPSAII assay is intended to be used in conjunction with the Atellica IM total PSA II (tPSAII) assay in men aged 50 years and older with total prostate-specific antigen (PSA) values between 4 ng/mL (µg/L) and 10 ng/mL (µg/L) and a digital rectal examination (DRE) non-suspicious for cancer to determine the percent free PSA value. The percent free PSA value can be used as an aid in discriminating between prostate cancer and benign prostatic disease. A prostate biopsy is required for the diagnosis of prostate cancer.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Atellica IM free PSA II (fPSAII) package insert.

V. DEVICE DESCRIPTION

The Atellica IM free PSA II (fPSAII) is a fully automated chemiluminescent sandwich immunoassay.

1. Device Components:

   Materials Provided:

   The Atellica IM fPSAII kit materials include:

   - The fPSAII ReadyPack primary reagent pack:
     - Lite Reagent: 5.0 mL/reagent pack. Mouse monoclonal anti-PSA antibody (~200 ng/mL) labeled with acridinium ester, bovine serum albumin (BSA), mouse IgG, bovine IgG, surfactant, and sodium azide (<0.1%).
     - Solid Phase: 10 mL/reagent pack. Mouse monoclonal anti-free PSA antibody (2.5 ng/mL) labeled with biotin and bound to streptavidin paramagnetic particles, BSA, mouse IgG, bovine IgG, surfactant, and sodium azide (<0.1%).
   - The Atellica IM fPSAII master curve and test definition
   - fPSAII CAL low calibrator: 2.0 mL/vial. After reconstitution, a low level of free PSA (human) in goat serum, sodium azide (<0.1%).
   - fPSAII CAL high calibrator: 2.0 mL/vial. After reconstitution, a high level of free PSA (human) in goat serum, sodium azide (<0.1%).
   - The Atellica IM fPSAII CAL calibrator assigned value sheet.

   Required materials but not provided:
   Atellica IM Analyzer – with additional system fluids to operate the system including Atellica IM Wash, Atellica IM Acid, Atellica IM Base, and Atellica IM Cleaner.

   Optional materials may be used but not provided:
   Atellica IM Multi-Diluent 2
   Atellica IM fPSAII MCM (master curve material)

2. Assay Principles and Procedures:

   The assay uses two monoclonal mouse antibodies in the Atellica IM fPSAII ReadyPack primary reagent pack. The Lite Reagent contains a monoclonal anti-PSA antibody labeled with acridinium ester, and an unlabeled free-PSA-specific monoclonal mouse anti-PSA antibody. The Solid Phase contains another monoclonal mouse anti-free PSA antibody labeled with biotin and bound to streptavidin paramagnetic latex particles. The sample is incubated with the Lite Reagent and Solid Phase simultaneously, and then the immune complex is washed. A direct relationship

exists between the amount of analyte present in the patient sample and the amount of relative light units (RLUs) detected by the system.

The Atellica IM fPSAII utilizes two-point calibration (Low Calibrator, High Calibrator) which are provided with the reagent kit. The calibration procedure is detailed in the package insert of the Atellica IM fPSAII.

The Atellica IM analyzer automatically performs the following steps:

- Dispenses 30 µL of sample into a cuvette.
- Dispenses 200 µL of Solid Phase and 100 µL of Lite Reagent, then incubates the mixture for 8 minutes at 37°C.
- Performs a wash sequence using Atellica IM Wash.
- Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base Reagent to initiate the chemiluminescent reaction.
- Reports results

3. Results Interpretation

The Atellica IM fPSAII measures free prostate-specific antigen in serum or plasma to aid in the discrimination of prostate cancer from benign conditions for men ≥50 years of age with an Atellica IM tPSAII result between 4–10 ng/mL, and a digital rectal examination result that is non-suspicious of cancer. The Atellica IM fPSAII result is used with an Atellica IM tPSAII result to calculate the percentage of free PSA (%fPSAII) based on a ratio ((free PSA/total PSA)×100) in the specimen. A single clinical cut-off of 22% for %fPSAII may be used.

The free PSA serum or plasma concentration result from the Atellica IM fPSAII should not be interpreted, regardless of the value, as definitive evidence for the presence or absence of prostate cancer. The results should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings. A free PSA ratio, i.e., %fPSAII, below 22% does not definitively indicate prostate cancer, as total PSA levels may rise due to benign prostatic hyperplasia, prostatitis, infections, or recent procedures. A prostate biopsy is required for the diagnosis of cancer.

4. Traceability

The Atellica IM free PSA II (fPSAII) is standardized to the WHO international standard 17/102.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternative practices and procedures that aid in the detection of prostate cancer, including physical examination using digital rectal examination (DRE) and diagnostic imaging by transrectal ultrasound (TRUS). Other devices for measuring total PSA, %free PSA, Prostate Health Index (*phi*), or multi-analytes (4Kscore Test) in

venous blood sample (serum or plasma) are currently available to aid in the detection of prostate cancer in conjunction with DRE information in men aged 50 years and older. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his physician to select the method that best meets expectations and lifestyle. Confirmation of prostate cancer is determined by biopsy.

VII. MARKETING HISTORY

The Atellica IM fPSAII has not been previously marketed in the United States.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

For the discrimination of prostate cancer from benign prostatic conditions, the free PSA result is used in conjunction with Atellica IM total PSAII (tPSAII) result to determine the %fPSAII, which is a ratio ((free PSA/total PSA)×100) of free PSA in the specimen. Free PSA assays are not indicated as the sole diagnostic tool to confirm the presence or absence of malignant prostatic disease. Free PSA concentrations, regardless of the value, should not be interpreted as definitive evidence for the presence or absence of prostatic cancer. A prostate biopsy is required for the diagnosis of cancer.

Subjects with a falsely low percent free PSA result could lead to an unnecessary biopsy. Before treatment, patients with confirmed prostate carcinoma frequently have levels of %fPSAII within the range observed in healthy individuals. Elevated levels of %fPSAII can be observed in patients with nonmalignant diseases. Specimens obtained from patients undergoing prostate manipulation, especially needle biopsy and transurethral resection, may show erroneously high results. Care should be taken if the fPSA and tPSA samples are drawn before these procedures are performed.

The concentration of fPSA in a given specimen determined with assays from different manufacturers can vary because of differences in assay methods, calibration, and reagent specificity. PSA in serum and in seminal fluid exists primarily in complexed and free forms, respectively. Quality control samples may be produced by introducing seminal fluid PSA into serum matrices. fPSA levels in these controls, determined with different manufacturers' assays, will vary depending on the method of standardization, antibody specificity, and different reactivity with complexed and free forms of PSA. Therefore, it is important to use assay-specific values to evaluate quality control results.

IX. SUMMARY OF NON-CLINICAL STUDIES

A. Precision:

Within-Laboratory Precision:
The within-laboratory precision was evaluated according to CLSI EP05-A3: *Evaluation of Precision Performance of Quantitative Measurement Methods – Third Edition*. A panel of six native human serum samples and three control samples, were tested in duplicate with two runs per day, for 20 days, using three separate lots on one Atellica IM instrument, producing a total of 80 measurements for each instrument-lot combination. The following components of imprecision were estimated for a single lot: within-run (repeatability), between-run, between-day, and within-laboratory. The mean (ng/mL), standard deviation (SD) (ng/mL) and percent coefficient of variation (%CV) results are summarized in Table 1 below.

Table 1. Within-Laboratory Precision of the Atellica IM fPSAII.

Sample	N	Mean (ng/mL)	Within-Run		Between-Run		Between-Day		Within-Laboratory	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum 1	80	0.06	0.004	6.7	0.002	3.3	0.002	3.3	0.005	8.4
Serum 2	80	0.34	0.007	2.1	0.002	0.6	0.008	2.4	0.011	3.2
Serum 3	80	0.98	0.018	1.8	0.012	1.2	0.024	2.4	0.032	3.3
Serum 4	80	2.10	0.029	1.4	0.031	1.5	0.054	2.6	0.069	3.3
Serum 5	80	10.17	0.143	1.4	0.180	1.8	0.210	2.1	0.311	3.1
Serum 6	80	19.69	0.246	1.2	0.276	1.4	0.409	2.1	0.551	2.8
Control 1	80	0.13	0.004	3.1	0.002	1.5	0.003	2.3	0.005	4.2
Control 2	80	3.92	0.056	1.4	0.081	2.1	0.081	2.1	0.128	3.3
Control 3	80	16.71	0.205	1.2	0.287	1.7	0.362	2.2	0.506	3.0

Lot-to-Lot Precision:
The lot-to-lot precision was evaluated by performing the same 20-day within-laboratory protocol described above on three lots of Atellica IM fPSAII reagents on one analyzer. The combined data for each sample on all three lots (N=240) were analyzed. The results are summarized in Table 2 below.

Table 2. Lot-to-Lot Precision of the Atellica IM fPSAII

Sample	N	Mean (ng/mL)	Within-Run		Between-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum 1	240	0.07	0.003	4.3	0.001	1.4	0.002	2.9	0.003	4.3	0.005	7.1
Serum 2	240	0.35	0.007	2.0	0.003	0.9	0.007	2.0	0.011	3.1	0.015	4.3
Serum 3	240	1.00	0.016	1.6	0.012	1.2	0.021	2.1	0.030	3.0	0.042	4.2
Serum 4	240	2.15	0.031	1.4	0.023	1.1	0.044	2.0	0.061	2.8	0.084	3.9

Serum 5	240	10.37	0.148	1.4	0.123	1.2	0.196	1.9	0.239	2.3	0.364	3.5
Serum 6	240	20.11	0.240	1.2	0.301	1.5	0.351	1.7	0.474	2.4	0.704	3.5
Control 1	240	0.13	0.004	3.1	0.001	0.8	0.003	2.3	0.005	3.8	0.007	5.4
Control 2	240	4.02	0.063	1.6	0.072	1.8	0.074	1.8	0.104	2.6	0.159	4.0
Control 3	240	17.05	0.265	1.6	0.277	1.6	0.313	1.8	0.350	2.1	0.606	3.6

Reproducibility:
A panel of five native human serum samples and three controls were tested at three different sites using three reagent lots and one instrument per laboratory site. The samples were tested in triplicates, with two runs per day, for five days, producing a total of 270 measurements for each sample. The reproducibility results for all lots and all sites combined are shown in Table 3 below.

Table 3. Site-to-Site Reproducibility of the Atellica IM fPSAII (n=270 per sample)

Sample	Mean (ng/mL)	Within-Run		Between-Run		Between-Day		Between-Lot		Between-Site		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Serum 1	0.41	0.008	2.0	0.005	1.2	0.006	1.5	0.002	0.5	0.013	3.2	0.017	4.1
Serum 2	0.98	0.016	1.6	0.014	1.4	0.010	1.0	0.001	0.1	0.023	2.3	0.033	3.4
Serum 3	2.51	0.037	1.5	0.041	1.6	0.019	0.8	0.000	0.0	0.079	3.1	0.098	3.9
Serum 4	9.46	0.129	1.4	0.136	1.4	0.079	0.8	0.000	0.0	0.046	0.5	0.209	2.2
Serum 5	14.66	0.236	1.6	0.158	1.1	0.195	1.3	0.000	0.0	0.240	1.6	0.420	2.9
Control 1	0.10	0.004	4.0	0.002	2.0	0.002	2.0	0.001	1.0	0.002	2.0	0.005	5.0
Control 2	3.30	0.057	1.7	0.050	1.5	0.040	1.2	0.036	1.1	0.038	1.2	0.100	3.0
Control 3	14.22	0.194	1.4	0.143	1.0	0.255	1.8	0.186	1.3	0.223	1.6	0.455	3.2

B. Detection Capability:

The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) studies were conducted according to CLSI EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement procedures*.

Limit of Blank (LoB)
The LoB was determined by testing four human female serum samples in six replicates per sample, twice a day, over a period of five days, using two Atellica IM analyzers and three reagent lots for a total of 480 measurements per reagent lot. The LoB was determined using a non-parametric approach, calculated as the 95th percentile of all values sorted from lowest to highest. The highest value across three lots was used to establish the LoB for the Atellica IM fPSAII device. The limit of blank of the Atellica IM fPSAII was determined to be 0.01 ng/mL.

Limit of Detection (LoD)
The LoD was determined by testing five serum samples with a low concentration of free PSA. The samples were evaluated using five replicates per sample, two runs per day for three days, using three reagent lots and one Atellica IM analyzer, for a total of

150 measurements per reagent lot. The LoD was determined using a non-parametric approach. The highest value across three lots was used to establish the LoD for the Atellica IM fPSAII. The limit of detection was determined to be 0.03 ng/mL.

Limit of Quantitation (LoQ)

The LoQ was evaluated using nine native human serum pools with free PSA concentrations ranging from 0.01 ng/mL to 0.30 ng/mL. The nine native serum pools were evaluated using four replicates, twice per day over a period of five days, using two Atellica IM analyzers and three reagent lots, for a total of 240 measurements per sample. The LoQ for each reagent lot was determined as the analyte concentration corresponding to 15% within-laboratory %CV or the LoD, whichever is greater. The highest value across three lots was used to establish the LoQ for the Atellica IM fPSAII. The limit of quantitation was determined to be 0.05 ng/mL.

The determined LoB/LoD/LoQ for the Atellica IM fPSAII is summarized in the following table.

Table 4. Detection capability for the Atellica IM fPSAII

	Limit of Blank (LoB)	Limit of Detection (LoD)	Limit of Quantitation (LoQ)
Atellica IM fPSAII	0.01 ng/mL	0.03 ng/mL	0.05 ng/mL

C. Linearity:

The linearity study was conducted according to CLSI EP06-Ed2: *Evaluation of the Linearity of Quantitative Measurement Procedures*. A twelve level dilution series was prepared using a high free PSA serum pool and a low free PSA serum pool, with free PSA ranging from 0.03 ng/mL to 29.00 ng/mL. The dilution levels were tested using five replicates each on one Atellica IM analyzer with three reagent lots. The expected values were calculated based on dilution scheme and predicted values were calculated using a weighted least squares regression analysis without an intercept. The percent deviation (%Deviation) from linearity was calculated for each level.

Table 5. Linearity of the Atellica IM fPSAII

Lot	Test range (ng/mL)	Slope (95% CI)	Range of %Deviation from Linearity
1	0.03 – 26.73	1.07 (1.06 – 1.09)	-6.8% to 2.2%
2	0.03 – 25.71	1.03 (1.02 – 1.05)	-3.8% to 4.9%
3	0.03 – 27.45	1.04 (1.04 – 1.05)	-4.2% to 0.7%

The Atellica IM fPSAII was determined to be linear from 0.03 – 25.71 ng/mL fPSA, which supports the analytical measuring interval (AMI) of 0.05 – 25.00 ng/mL fPSA.

D. High-Dose Hook Effect:

A study was conducted to evaluate the hook effect of the Atellica IM fPSAII. A high fPSA sample was prepared by spiking non-complexing PSA into human female serum to a target concentration of approximately 13,000 ng/mL. Nine dilutions of the high sample were prepared using multi-diluent 2, which is the recommended diluent for patient samples above the analytical measuring range. All samples were tested with three replicates using three reagent lots and one Atellica IM analyzer. The data was analyzed by plotting the actual mean instrument response (RLUs) versus the expected dose (ng/mL) of the samples. No hook effect was observed up to 10,000 ng/mL.

E. Automated Dilution

The Atellica IM fPSAII has an automated dilution function when the patient sample results in a value that exceeds the upper limit of the analytical measuring interval (result is ">25 ng/mL"). A study was performed according to CLSI EP34-Ed1: *Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking* to evaluate the effect of auto-dilution on the performance of the Atellica IM fPSAII with Atellica IM Multi-Diluent 2. A high fPSA stock was prepared by spiking non-complexing PSA (11,000 ng/mL) into a male serum base pool (8.25 mg/mL) to prepare 10 sample pools above the fPSAII measuring interval. The samples were measured using four replicates per sample, three Atellica IM fPSAII reagent lots, two Atellica IM Analyzers, one lot of Multi-Diluent 2, and 1:2 and 1:5 dilutions. The percent recovery was calculated for each sample and dilution level. The results support the function of the 1:2 and 1:5 auto-dilution feature using Atellica IM Multi-Diluent 2.

F. Assay Reportable Range:

Analytical Measuring Interval:
The results from the LoQ, precision, and linearity studies support an analytical measuring interval of 0.05 – 25.00 ng/mL for the Atellica IM free PSA II (fPSAII).

Extended Measuring Interval:
The results from the LoQ, precision, linearity, and automated dilution studies support an extended measuring interval of 0.05–125.00 ng/mL using Atellica IM Multi-Diluent 2 with 1:2 and 1:5 dilution schemes.

G. Analytical Specificity/Interference

1. Endogenous and Exogenous Interference

   Interference testing was conducted in accordance with CLSI EP07-Ed3: *Interference Testing in Clinical*. Four serum pools at 0.34 ng/mL, 1.14 ng/mL, 2.74 ng/mL, and 19.39 ng/mL fPSA, or two serum pools at 0.40 ng/mL, and 15.0 ng/mL, were spiked with endogenous or exogenous interferents at the concentrations indicated in Table 6 and Table 7 below. For each potential interfering substance,

"control" samples were prepared by spiking with the appropriate diluents at the same volume as the interfering substance, and "test" samples were prepared by spiking interferent at the concentration indicated. All samples were tested on one Atellica IM instrument using one reagent lot, with three replicates per sample. The percent interference was calculated using the following equation:

$$\%Interference = ((Test - Control)/Control) \times 100$$

For endogenous substances, no significant interferences, defined as within ±10% interference, was observed up to the concentrations listed below.

Table 6. Endogenous Interferences

Substance	Concentration
Bilirubin (Unconjugated)	60 mg/dL
Bilirubin (Conjugated)	40 mg/dL
Hemoglobin	1000 mg/dL
Human IgG	2.5 g/dL
Lipemia (Intralipid)	3300 mg/dL
Total Protein	15 mg/dL
Cholesterol	500 mg/dL
Rheumatoid Factor	1500 IU/mL

For exogenous substances, no significant interferences (%Interference within ±10%) were observed in the study up to the concentration listed below.

Table 7. Exogenous Interferences

Substance	Concentration	Substance	Concentration
Biotin	3500 ng/mL	Goserelin acetate	7.2 µg/mL
Silwet L720	30 mg/mL	HAMA*	2640 µg/L
Acetaminophen†	15.6 mg/dL	Hydrochlorothiazide†	0.113 mg/dL
Acetylsalicylic Acid†	3.0 mg/dL	Ibuprofen†	21.9 mg/dL
Alfuzosin hydrochloride	12 µg/ml	Ketoconazole†	0.620 mg/dL
Alprazolam†	0.258 mg/dL	Leuprolide acetate	10.0 mg/dL
Amlodipine Besylate†	0.0075 mg/dL	Lisinopril†	0.0246 mg/dL
Aminoglutethimide	72 µg/mL	Megestrol acetate	250 µg/mL
Amoxicillin Trihydrate†	5.40 mg/dL	Metformin HCl†	1.20 mg/dL
Atorvastatin†	0.075 mg/dL	Methotrexate	300 mg/dL
Casodex (bicalutamide)	60 µg/mL	Mitomycin C	100 µg/mL
Cimetidine†	3.0 mg/dL	Naproxen Sodium†	36.0 mg/dL
Ciprofloxacin†	1.2 mg/dL	Nitrofurantoin†	0.213 mg/dL
Cisplatin dichloride	0.25 mg/mL	Novantrone	0.5 mg/mL
Clomipramine HCl†	0.270 mg/dL	Omeprazole†	0.840 mg/dL
Cyclophosphamide	800 µg/mL	Oxaliplatin	0.25 mg/mL
Diethylstilbestrol	25 µg/mL	Paclitaxel	4 ng/mL
Docetaxel	5.5 µg/mL	Prazosin hydrochloride	85 ng/mL

Substance	Concentration	Substance	Concentration
Doxazosin mesylate	4.0 µg/mL	Prednisone	1.65 µg/mL
Doxorubicin hydrochloride	7.0 mg/dL	Sildenafil citrate	0.2 mg/mL
Doxycycline Hyclate†	1.8 mg/dL	Sulfamethoxazole†	40.5 mg/dL
Dutasteride	0.3 µg/mL	Terazosin HCl	1.45 mg/mL
Estramustine phosphate	20 mg/dL	Trimethoprim†	4.20 mg/dL
Finasteride	25 µg/mL	Triptorelin	28 ng/mL
Flomax	1.0 µg/mL	Vinblastine sulfate salt	12 µg/mL
5'-Fluorouracil	1.6 mg/mL	Vincristine sulfate salt	1.0 mg/mL
Fluoxetine HCl†	0.142 mg/dL	Warfarin HCl†	7.50 mg/dL
Flutamide	1.0 mg/dL	Zoledronic acid	667 ng/mL
Furosemide†	1.59 mg/dL		

* Human anti-mouse antibodies.

† These interferants were tested using two serum pools and five replicates per sample.

2. Cross-Reactivity

The cross reactivity of the Atellica IM fPSAII was assessed according to the recommendations contained in CLSI EP07-Ed3. Four human serum pools with fPSA concentrations of 0.40 ng/mL, 1.00 ng/mL, 2.50 ng/mL, and 18.50 ng/mL free PSA were prepared and spiked with cross-reactants to prepare cross-reactant-test and control samples. All samples were tested with three replicates for complexed PSA (PSA-ACT), Kallikrein, and Prostatic Acid Phosphatase (PAP), or five replicates for Ferritin, Prolactin, Carcinoembryonic Antigen (CEA), Human Chorionic Gonadotropin (HCG), and Alpha-fetoprotein (AFP). None of the cross-reactants exceeded 2% interference or bias to the Atellica IM fPSAII for the tested concentrations shown below.

Table 8. Cross-Reactivity of the Atellica IM fPSAII

Substance	Concentration
Alpha-fetoprotein (AFP)	10,000 ng/mL
Carcinoembryonic Antigen (CEA)	200 ng/mL
CA 19-9	1000 U/mL
Ferritin	10,000 ng/mL
Human Chorionic Gonadotropin (HCG)	10,000 mIU/mL
Human Kallikrein	100 µg/mL
Prolactin	500 ng/mL
Prostatic Acid Phosphatase (PAP)	1000 ng/mL

3. Anti-Nuclear Antibodies (ANA) interference

For ANA testing, serum samples from ANA positive individuals (confirmed positive [≥1.0 AI] status by the Bio-Rad ANA screening assay) were obtained from a commercial vendor. Samples were screened for endogenous free PSA and then

spiked with additional free PSA to prepare serum samples with free PSA concentrations of 0.4 ng/mL, 1.0 ng/mL, 2.5 ng/mL, and 15 ng/mL free PSA. ANA positive samples, spiked with PSA or unspiked, and ANA negative serum samples, spiked with PSA or unspiked, were evaluated using five replicates, one reagent lot, and one Atellica IM analyzer. The difference in PSA concentration of the spiked vs unspiked ANA positive samples (test) was compared to the difference between the spiked and unspiked serum samples (control). ANA did not affect the expected results, indicating no interference.

H. Matrix Comparison

The equivalency of using K2 EDTA and lithium heparin plasma and serum for the Atellica IM fPSAII was assessed in accordance with CLSI EP35-Ed1, *Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures*. 92 matched samples were collected in serum separator tubes (SST) and plasma (K2-EDTA and lithium heparin) tubes from men over 50 years of age. Each sample was tested in singlicate using one reagent lot and one Atellica IM instrument. Matched samples with measured values below the LoQ (0.05 ng/mL) or an insufficient sample volume were excluded from the analysis. Slope and Y-intercept results were calculated using a Weighted Deming regression analysis. The results are presented below.

Table 9. Matrix comparison of the Atellica IM fPSAII

Matrix comparison	N	Range (ng/mL)	Slope (95% CI)	Y-Intercept (95% CI)	Correlation
K2EDTA vs Serum	84	0.05 – 23.18	0.97 (0.93; 1.00)	0.01 (-0.01; 0.03)	0.990
Lithium Heparin vs Serum	85	0.06 – 23.18	0.94 (0.89; 1.00)	0.00 (-0.03; 0.04)	0.996

I. Stability

1. Kit Stability

a. Atellica IM fPSAII Reagent Pack:

The shelf-life of the Atellica IM fPSAII ReadyPack reagent pack was established by testing five native serum samples or pools with free PSA concentrations of 0.37 ng/mL, 1.00 ng/mL, 2.00 ng/mL, 10.00 ng/mL, 20.00 ng/mL, with three different reagent lots stored at 2-8°C. The ongoing real-time shelf-life study will test the following timepoints: Day 0 (T0), 1 month, 3 months, 6 months, 7 months, 9 months, 10 months, 12 months, 13 months, 15 months, 18 months, 21 months, 23 months, 24 months, and 25 months. At each timepoint, the samples are tested with five replicates per lot on two different Atellica IM analyzers. The available stability results across three different lots currently demonstrate that the Atellica IM fPSAII reagent kit is stable for six months when stored at 2-8°C.

The onboard stability (OBS) of the Atellica IM tPSAII ReadyPack reagent pack was established by testing five native patient samples with two different regent lots stored on one Atellica IM analyzer. At each timepoint, a fresh reagent pack was run alongside reagent packs that remained on the system for the duration of the study. The onboard pack results were compared to the results of the fresh reagent pack. All samples were tested in five replicates on the "fresh" packs and three replicates with one replicate per pack on the "open" packs on days 0, 7, 14, 21, 28, 29, and 34. For the lot calibration interval, all samples were tested in five replicates on the “fresh” reagent packs on days 0, 7, 14, 21, 28, 29, 34, 54, 55, and 56. Stability results across two different lots demonstrated reagent onboard stability for 28 days, pack calibration interval for 28 days, and lot calibration interval of 42 days.

b. fPSAII CAL (Calibrators)

The study was done to determine the stability of the fPSAII CAL high and low calibrators at the following conditions:

- Shelf life (unopened): Testing was established along with the shelf-life stability of the reagent pack as shown above. The available stability results currently demonstrate that the Atellica IM fPSAII calibrators are stable for six months when stored at 2-8°C.
- Onboard the Atellica IM Analyzer at ambient temperature: testing was done at the baseline point, followed by subsequent testing at 2, 4, 6, 8, and 9 hours using two different lots, in replicates of five across two different lots. The results demonstrate that Atellica IM fPSAII calibrators are stable for 8 hours when stored onboard the Atellica IM analyzer.
- Opened vials stored in refrigerator at 2-8°C: testing was done at baseline point (Day 0), then tested at days 7, 14, 21, 28, 29, 30, and 32 in replicates of five across two different lots. The results demonstrate that the Atellica IM fPSAII calibrators are stable for 30 days when stored at 2-8ºC.

c. Multi-diluent 2 (MDIL-2)

A study was done to determine the shelf-life and onboard stability for Multi-diluent 2 (MDIL-2) which is used in auto-dilution for high patients sample out of the measuring range. Patient samples with fPSA above the upper limit of measuring interval were tested at 1:2 and 1:5 dilutions using MDIL-2.

- Shelf life: the one lot of Atellica MDIL-2 was evaluated at baseline or stored at 2-8°C for 6 months, 18 months, or 22 months. The lots were evaluated using one native serum sample (44 ng/mL fPSA) and tested with five replicates on one Atellica IM Analyzer. The results demonstrate that the Atellica IM Multi-Diluent 2 is stable for 18 months when stored unopened at stored at 2-8°C.
- Onboard: the two native serum pools were tested in triplicate using two lots of the MDIL2 packs which remained on the system for the duration of

the study at timepoints up to 32 days. The onboard MDIL2 auto-dilution results were compared with day-zero MDIL2 auto-dilution results at each timepoint. The results demonstrate that the Atellica IM Multi-Diluent 2 is stable for 28 days when stored onboard the Atellica IM analyzer.

The claimed kit stability for the Atellica IM fPSAII is summarized below.

Table 10. Stability for the Atellica IM fPSAII

Kit Component	Storage	Stability Claim
fPSAII ReadyPack Reagent Pack	Unopened/Shelf-life	6 months at 2-8ºC*
	Onboard/In-Use	28 days
fPSAII CAL (calibrators)	Unopened/Shelf-life	6 months at 2-8ºC*
	Open Vial	30 days at 2-8ºC
	Onboard	8 hours
Multi-Diluent 2 (MDIL-2)	Unopened/Shelf-life	18 months at 2-8ºC
	Onboard	28 days

* The real-time shelf-life study is currently ongoing. The available results support the indicated claim.

2. Specimen Stability

Blood was collected from 10-11 men using four tube types (red top serum, SST, K2-EDTA, lithium heparin). The samples were tested in the range from ~0.12 ng/mL to ~19.7 ng/mL of free PSA. Studies 1 and 2 assessed unprocessed samples at room temperature (0, 8, 24, 48, and 72 hours) and processed samples on-clot at 2-8°C in primary tubes (0, 8, 24, 48, and 144 hours); Studies 3 and 4 examined separated samples in secondary containers at room temperature (20-25°C) (0, 8, 9, 16, 24, 39, 48, and 54 hours) and refrigerated (2-8°C) (0, 24, 39, 48, 54, and 72 hours); Studies 5 and 6 evaluated frozen storage at -80°C (0, 1, 3, 6, 12, and 15 months) and freeze/thaw cycles (1-4 cycles) (0, 1, 2, 3, and 4 freeze/thaw cycles). All samples were tested in triplicate using one reagent lot, with percent bias calculated relative to baseline T0 measurements to assess stability over time. The stability of specimens is summarized in the table below.

Table 11. Stability for Specimens used for the Atellica IM fPSAII

Stability Conditions	Stability Claim
On clot	8 hours at 18-25ºC
Time to centrifugation	8 hours at 2-8ºC
In secondary tube	8 hours at 18-25ºC
	48 hours at 2-8ºC
	12 months at -80ºC
Freeze/Thaw	Up to 2 cycles

X. SUMMARY OF PRIMARY CLINICAL STUDY

A multicenter prospective clinical study was conducted at 26 clinical sites across the United States to evaluate the clinical performance the Atellica IM fPSAII. The study included 1237 men aged 50 years or older who were referred to a urologist for the evaluation of prostate cancer. All included subjects had an Atellica IM tPSAII of 4–10 ng/mL (µg/mL), and DRE findings non-suspicious of cancer. In addition to the geographic distribution of collection sites where specimens were collected, the subjects were also distributed across racial and ethnic groups, age categories, and family history status.

A summary of the clinical study is presented below.

A. Study Design

The clinical performance of the Atellica IM fPSAII was evaluated in a multicenter prospective clinical study. The study involved an analysis of 1237 samples from men aged 50 years of age or older, who had been referred to a urologist for an evaluation of the presence of prostate cancer. The samples were collected from 26 clinical sites in geographically diverse areas across the United States under an IRB approved protocol and with informed consent. Enrolled in the clinical performance study were men presenting to a practicing urologist with symptoms resulting in an evaluation for prostate cancer, including trans-rectal prostate biopsy, who have total PSA results between 4.0 and 10.0 ng/mL inclusive and whose digital rectal examination (DRE) results were not suspicious for cancer.

1. Inclusion and Exclusion Criteria

   Enrollment in the study was limited to patients who met the following inclusion criteria:

   - Subject must be male and age 50 or older.
   - Subject must understand and sign informed consent prior to any study procedure.
   - Subject must be entered into this study only once.
   - Specimens must have a ADVIA Centaur PSA value of 2.0 to 11.0 at the time of study collection.
   - Subject must have had a DRE either more than 5 days but within 20 days prior to study blood draw, or, will have a DRE within 30 days after study blood draw.
   - Subject must have a DRE result that is non-suspicious for prostate cancer.
   - Subjects must have auditable medical records available to verify required medical information.
   - Subject must have a prostate biopsy within 60 days, after study blood draw, and the results must be known.
   - If the biopsy results are positive for prostate cancer, clinical stage must be determined and Gleason score should be provided, if available.

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Subject with history of prostate cancer prior to study blood draw.
- Subject who has undergone any form of treatment or procedure(s) for prostate disease known to impact PSA levels, including but not limited to prostate biopsy, prostate radiation, catheterization within 90 days prior to study blood draw.
- Subject who has taken medication for prostate disease within 90 days prior to study blood draw within the following classes of medication known to impact PSA levels: 5α-reductase inhibitors, anti-androgens, androgen therapy or hormone therapy (use of alpha blockers is allowed).
- Subject had study specimens collected other than serum.
- Subject failed to meet any inclusion criteria.

2. Follow-up Schedule

No follow-up schedule was required for the enrolled subjects. All subjects were prospectively enrolled, based on the normal flow of patients scheduled to receive a prostate biopsy at each site.

3. Clinical Endpoints

The clinical performance of the Atellica IM fPSAII test using percent free PSA cutoffs of 22.0% as a single free PSA cutoff, as well as 21.0%, 23.0%, 25.0%, 27.0%, and 30.0%, in comparison to biopsy results was evaluated. Performance measures were calculated for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The data should demonstrate that the Atellica IM free PSA II test is a statistically informative test: True Positive rate (sensitivity) > False Positive rate (1-specificity) or equivalently, PPV >prevalence and NPV >1-prevalence).

The Atellica IM fPSAII is used in conjunction with DRE and the Atellica IM tPSAII. In the tPSA range of 4–10 ng/mL (µg/L), the percent free PSA (fPSA/total PSA x 100) should provide additional clinical value beyond the Atellica IM tPSAII results alone, reflected by:

i) Statistically significant increase in the probability of positive biopsy for subjects with (DRE negative, Atellica IM tPSAII results between 4–10 ng/mL, <22% fPSAII) results in comparison to the subjects with DRE negative and Atellica IM tPSAII results between 4–10 ng/mL only.
ii) Statistically significant decrease in the probability of a positive biopsy results for the subjects with (DRE negative, Atellica IM tPSAII results between 4–10 ng/mL, and >22% fPSAII) results compared to the subjects with DRE negative and Atellica IM tPSAII results between 4–10 ng/mL only.

B. Accountability of PMA Cohort

The pivotal clinical performance study includes 1,333 eligible subjects with Atellica IM tPSAII results between 4-10 ng/mL from 26 geographically diverse urology clinics in the U.S. All subjects are aged 50 years or older who underwent local PSA testing in conjunction with DRE and were referred to a urologist for evaluation of prostate cancer. Of the 1,333 eligible subjects, 96 subjects were excluded, including: one incomplete case report form, 86 due to protocol deviations, and nine subjects due to samples that were unavailable for testing. This resulted in 1,237 subjects that were included in the clinical performance evaluation of the Atellica IM fPSAII.

C. Study Population Demographics and Baseline Parameters

The distributions of demographic and clinical characteristics of the 1,237 subjects are described in the table below.

Table 12. Distribution of Demographic and Clinical Information for the Study Population

Demographic/Clinical Characteristics		Total N=1237 n (%)
Race, Ethnicity	White	1047 (84.6%)
	African American	93 (7.5%)
	Asian	14 (1.1%)
	Other	6 (0.5%)
	Unknown	75 (6.1%)
Age Group	50 – 59	300 (24.3%)
	60 – 69	611 (49.4%)
	70 – 85	326 (26.3%)
DRE	Abnormal	0 (0%)
	Normal	1237 (100%)
Biopsy Result	Negative	556 (44.9%)
	Gleason 6	255 (20.6%)
	Gleason 7 (3+4)	241 (19.5%)
	Gleason 7 (4+3)	103 (8.3%)
	Gleason 8	53 (4.3%)
	Gleason 9	26 (2.1%)
	Gleason 10	3 (0.2%)

The following table describes the distributions of fPSAII, tSAII, and percent fPSA for patients with prostate cancer and benign prostatic disease.

Table 13. The value of fPSAII, tPSAII, and %fPSAII Samples Statistics by Biopsy

Assay	Biopsy	N	Median (ng/mL)	Mean (ng/mL)	SE* of Mean (ng/mL)
fPSAII (ng/mL)	Benign	556	0.98	1.08	0.02
	Prostate Cancer	681	0.79	0.86	0.02
tPSAII (ng/mL)	Benign	556	6.103	6.350	0.067
	Prostate Cancer	681	6.124	6.436	0.061
%fPSAII	Benign	556	15.86	17.21	0.32
	Prostate Cancer	681	12.33	13.61	0.24

*SE: Standard Error

D. Safety and Effectiveness Results

1. Safety Results

Atellica IM fPSAII involves testing venous whole blood samples. These specimens are routinely taken as part of the practice of medicine and, therefore, sample collection presents no additional safety hazard to the patient being tested.

The diagnosis of prostate cancer must be confirmed by biopsy. When using the Atellica IM fPSAII, subjects with falsely low percent free PSA ratio result could lead to an unnecessary biopsy. Subjects with falsely high percent free PSA ratio result may not receive a necessary biopsy, which could delay recognition of the presence of prostate cancer by the physician and could adversely delay the initiation of therapy. The safety concern with respect to biopsy is often associated with infectious complications following the procedure.

In the pivotal clinical performance study, all enrolled subjects were men presenting to a practicing urologist with symptoms that would lead to an evaluation for prostate cancer and who are scheduled to receive a prostate needle biopsy. The Atellica IM fPSAII result for these subjects did not alter the medical decision for these subjects, therefore, present no additional safety hazard to the subjects being tested.

2. Effectiveness Results

The analysis of effectiveness was based on the 1,237 evaluable patients enrolled at 26 urology clinics in the U.S. The performance of Atellica IM fPSAII as an aid in discriminating between prostate cancer and benign prostatic disease cancer were evaluated using a percent free PSAII (%fPSAII) ranges, or a single %fPSAII cut-off (i.e., 22%), in comparison to the clinical diagnosis of prostate cancer for each subject. The clinical diagnosis of prostate cancer was based on the pathological examination of prostate biopsy tissues, yielding a Gleason Score 6 or greater. All other findings were grouped as non-cancer.

Poolability of data analysis:

The evaluable data were collected from 26 sites across the U.S. The poolability of the data from different sites was evaluated based on the prevalence of prostate cancer, age of subjects, tPSAII, fPSAII, and the %fPSAII results.

i) The prevalence of prostate cancer in the study was 55.05% and the site-specific cancer prevalence ranged from 0.00% to 100.00% for all sites, and 40.0% to 68.75% for sites with more than 5 total subjects.
ii) The mean age of the study cohort was 65.0 years with the site-specific mean age ranging from 62.1 to 79.0 years.
iii) The mean Atellica IM tPSAII test value was 6.400 ng/mL, and the site-specific mean of total PSA ranged from 4.435 to 7.514 ng/mL.
iv) The mean Atellica IM fPSAII test value was 0.96 ng/mL, and the site-specific mean of free PSA ranged from 0.62 to 1.57 ng/mL.
v) The mean percent free PSA ratio (%fPSAII) was 15.23%, and the site-specific mean %fPSAII ranged from 10.57 to 29.09%.

Based on the above evaluation, the performance of the Atellica IM fPSAII test is evaluated using the pooled data across 26 sites.

Results

The clinical performance of the Atellica IM fPSAII was determined in a clinical performance study involving the analysis of 1,237 samples from men 50 years of age or older with an Atellica IM tPSAII result between 4 and 10 ng/mL, and non-suspicious of prostate cancer by DRE. In the total PSA range of 4–10 ng/mL, the lower the percentage of fPSA (fPSA/tPSA x 100%), the higher the risk of prostate cancer. The probability of detecting prostate cancer upon biopsy by age and percent fPSAII (%fPSA) is shown below.

Table 14. Probability of Detecting Prostate Cancer Based on Biopsy by Age

%fPSAII	50–64 years		≥65 years		All ages	
	% of Cancers (n/N)	95% CI*	% of Cancers (n/N)	95% CI*	% of Cancers (n/N)	95% CI*
≤ 10%	61.4 (97/158)	53.8–68.6	82.1 (115/140)	75.0–87.6	71.1 (212/298)	65.8–76.0
>10–15%	47.1 (96/204)	40.3–53.9	70.1 (143/204)	63.0–76.0	58.6 (239/408)	53.7–63.3
>15–20%	40.5 (47/116)	32.0–49.6	53.0 (79/149)	45.0–60.9	47.5 (126/265)	41.6–53.6
>20–25%	56.8 (21/37)	40.9–71.3	43.5 (47/108)	34.6–52.9	46.9 (68/145)	39.0–55.0
>25%	14.0 (6/43)	6.6–27.3	38.5 (30/78)	28.4–49.6	29.8 (36/121)	22.3–38.4

* 95% confidence interval

Table 15. Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of the Atellica IM fPSA II

%fPSAII Cut-off	Sensitivity (n/N) (95% CI)	Specificity (n/N) (95% CI)	PPV (n/N)	NPV (n/N)
<21%	87.2% (594/681) (84.5 – 89.5%)	25.5% (142/556) (22.1 – 29.3%)	58.9% (594/1008)	62.0% (142/229)
<22%	90.5% (616/681) (88.0 – 92.4%)	21.2% (118/556) (18.0 – 24.8%)	58.4% (616/1054)	64.5% (118/183)
<23%	92.5% (630/681) (90.3 – 94.3%)	19.1% (106/556) (6.0 – 22.5%)	58.3% (630/1080)	67.5% (106/157)
<25%	94.7% (645/681) (92.8 – 96.2%)	15.3% (85/556) (12.5 – 18.5%)	57.8% (645/1116)	70.2% (85/121)
<27%	95.9% (653/681) (94.1 – 97.1%)	9.5% (53/556) (7.4 – 12.3%)	56.5% (653/1156)	65.4% (53/81)
<30%	97.7% (665/681) (96.2 – 98.5%)	6.1% (34/556) (4.4 – 8.4%)	56.0% (665/1187)	68.0% (34/50)

In the intended use population (N=1237), a %fPSAII cut-off of <22% yielded a sensitivity of 90.5% (616/681) (95% CI: 88.0 – 92.4%) and specificity of 21.2% (118/556) (95% CI: 18.0 – 24.8%).

If the tPSAII is used at a hypothetical cutoff for which the sensitivity of the %fPSAII and the tPSAII are the same (i.e., 90.5%), then the specificity of the tPSAII was 12.2% (68/556). Therefore, the %fPSAII provides a 9% (50/556) (95% CI: 6.9 – 11.7%) improvement in specificity over the tPSAII specificity. These results demonstrate that an additional 9% of men with benign prostatic disease may avoid unnecessary prostate biopsy when using %fPSAII over tPSAII.

To conclusively establish prostate cancer versus benign disease, all patients underwent a transrectal prostate biopsy. Thus, the set of subjects included in the clinical performance study may not fully represent a population where fPSA would be used for detection of prostate cancer since the performance of fPSA in a population of men who do not undergo biopsy for detection of prostate cancer was not evaluated.

3. Subgroup Analyses

Increased prevalence and severity of prostate cancer are well documented for African American men in the United States. The clinical performance of the Atellica IM fPSAII in the detection of prostate cancer (Gleason score ≥6) stratified by race/ethnicity is shown in the following table.

Table 16. Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of the Atellica IM fPSA II for White (N = 1047 men; 55.1% prevalence) and African American (AA) Men (N = 93 men; 64.5% prevalence).

%fPSAII Cut-off	Race	Sensitivity (n/N) (95% CI)	Specificity (n/N) (95% CI)	PPV (n/N)	NPV (n/N)
<21	White	87.2% (503/577) (84.2-89.7%)	26.8% (126/470) (23.0-31.0%)	59.4% (503/847)	63.0% (126/200)
	AA	83.3% (50/60) (72.0-90.7%)	18.2% (6/33) (8.6-34.4%)	65.0% (50/77)	37.5% (6/16)
<22	White	90.0% (519/577) (87.2-92.1%)	21.9% (103/470) (18.4-25.9%)	59.6% (519/866)	64.0% (103/161)
	AA	91.7% (55/60) (81.9-96.4%)	15.2% (5/33) (6.7-30.9%)	66.3% (55/83)	50.0% (5/10)
<23	White	92.0% (531/577) (89.5-94.0%)	19.8% (93/470) (16.4-23.6%)	58.5% (531/908)	66.9% (93/139)
	AA	93.3% (56/60) (84.1-97.4%)	12.1% (4/33) (4.8-27.3%)	65.9% (56/85)	50.0% (4/8)
<25	White	94.3% (544/577) (92.1-95.9%)	16.2% (76/470) (13.1-19.8%)	58.0% (544/938)	69.7% (76/109)
	AA	95.0% (57/60) (86.3-98.3%)	12.1% (4/33) (4.8-27.3%)	66.3% (57/86)	42.8% (3/7)
<27	White	95.7% (552/577) (93.7-97.1%)	10.4% (49/470) (8.0-13.5%)	56.7% (552/973)	66.2% (49/74)
	AA	95.0% (57/60) (86.3-98.3%)	3.0% (1/33) (0.5-15.3%)	64.0% (57/89)	25.0% (1/4)
<30	White	97.6% (563/577) (96.0-98.6%)	6.6% (31/470) (4.7-9.2%)	56.2% (563/1002)	68.9% (31/45)
	AA	96.7% (58/60) (88.6-99.1%)	0.0% (0/33) (0.0-10.4%)	63.7% (58/91)	0.0% (0/2)

4. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population. The device is indicated to be used in the population of men 50 years and older.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal

clinical study included three investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Not applicable.

XIII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Immunology Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The analytical performance studies support that the test can quantitatively measure free PSA levels from 0.05 ng/mL to 25.0 ng/mL using serum and plasma samples. The clinical effectiveness of the Atellica IM fPSAII was demonstrated by testing 1237 subjects at 26 different sites within the U.S. The Atellica IM fPSAII single cut-off of <22% yielded a sensitivity of 90.5% (616/681) (95% CI: 88.0 – 92.4%) and specificity of 21.2% (118/556) (95% CI: 18.0 – 24.8%). These results demonstrate that 90.5% of prostate cancers were correctly identified in the study population while 21.2% of men without prostate cancer were correctly identified. In comparison to the use of Atellica IM tPSAII results alone, the use of the Atellica IM fPSAII resulted in a 9% (95% CI: 6.9 – 11.7%) improvement in specificity for men with Atellica IM tPSAII results between 4–10 ng/mL and a DRE non-suspicious result.

The results from both the non-clinical and clinical studies indicate that the Atellica IM fPSAII is safe and effective for the in vitro quantitative measurement of free PSA and %fPSA in human adult serum and plasma (EDTA and Lithium Heparin) in conjunction with the Atellica IM tPSAII.

B. Safety Conclusions

The risks of the device are based on analytical performance testing as well as data collected in a clinical performance study conducted to support PMA approval as described above. As a diagnostic test, the Atellica IM fPSAII involves the collection of

blood from an individual for testing purposes and is to be performed by trained healthcare professionals with a CLIA moderate complexity testing certificate.

C. Benefit-Risk Determination

Assessment of Benefit:

The Atellica IM fPSAII is not a standalone diagnostic test or a standalone cancer screening test. It is indicated to be used as an aid in discriminating between prostate cancer and benign prostatic disease in men aged 50 years and older with total prostate-specific antigen (tPSA) values between 4 ng/mL and 10 ng/mL, and a digital rectal examination (DRE) nonsuspicious for cancer. In this setting, the output of the device/test is likely to be used clinically to help inform the decision as to whether to perform a prostate biopsy for patients with elevated total PSA values and nonsuspicious DRE findings. In some patients this will result in a benefit which may include increased cure rates related to early diagnosis of prostate cancer. In other patients, such as those with a total PSA between 4 – 10 ng/mL but with a negative %fPSAII result (>22% fPSAII), the use of the Atellica IM fPSAII may result in less morbidity due to the elimination of unnecessary biopsies, thereby resulting in a better quality of life. In summary, the clinical benefits of the Atellica IM fPSAII allow physicians to consider timely diagnostic or therapeutic options for the medical condition/disorder under evaluation.

The above assessment is based on the clinical performance results. The Atellica IM fPSAII single cut-off of <22% yielded a sensitivity of 90.5% (616/681) (95% CI: 88.0 – 92.4%) and specificity of 21.2% (118/556) (95% CI: 18.0 – 24.8%). These results demonstrate that 90.5% of prostate cancers were correctly identified in the study population while 21.2% of men without prostate cancer were correctly identified. The sensitivity of the Atellica IM fPSAII is clinically beneficial as the results demonstrate that the majority of prostate cancers were correctly identified for the intended use population. The Atellica IM fPSAII specificity (i.e., 21.2% (118/556) (95% CI: 18.0 – 24.8%)) is relatively low, but in comparison to the specificity of the Atellica IM tPSAII (i.e., 12.2% (68/556)), the use of the Atellica IM fPSAII resulted in a 9% (50/556) (95% CI: 6.9 – 11.7%) improvement in specificity. The 9.0% improvement in specificity provides significant evidence that the fPSAII ratio, when used in conjunction with tPSAII results, was more effective in discriminating benign prostatic disease from prostate cancer.

Assessment of Risk:

False positive and false negative results may introduce risks associated with the use of the Atellica IM fPSAII. An error producing a falsely elevated %fPSAII result could lead to a delay in the diagnosis of prostate cancer by the physician and could adversely delay the initiation of therapy. An error producing a falsely low %fPSAII result could lead to an unnecessary biopsy procedure. However, when the Atellica IM fPSAII is used according to the instructions provided, accurate results should be obtained.

As the use of the PSA test will result in a decision to perform a prostate biopsy in some patients, in addition to the relatively low direct risks of the biopsy procedure, there are risks of diagnosing ("over diagnosing") a low-risk prostate cancer which is much less likely to progress (likely a Gleason 6 cancer) in addition to the risks of missing a significant cancer (likely a Gleason 7 or higher). A falsely high %fPSAII ratio result may occur in specimens obtained from patients undergoing prostate manipulation, especially needle biopsy and transurethral resection, resulting in a missed or delayed diagnosis of prostate cancer. This is currently a controversial area, but these risks are widely understood in the medical community and are typically transmitted to patients with relevant decisions to make. Additionally, the limitations of the Atellica IM fPSAII are provided within the Atellica IM fPSAII labeling to alert physicians to conditions and situations that may contribute to the potential risk of false positive or false negative results. The result of this test is one of many factors that will be considered in the decision to do a biopsy.

Assessment of Benefit-Risk Balance:

For an individual patient, the benefit-risk balance is variable, with high uncertainty, and varies depending on many known and unknown factors. The current standard-of-care for the evaluation of men over the age of 50 years with respect to measuring total PSA, free PSA, and deciding whether to perform a prostate biopsy is based on the process of "shared decision-making." This is a highly individualized process between the patient and the physician and takes many factors into account, including personal risk factors such as age, ethnicity, family history, personal habits, expected longevity, tolerability of certain treatments and acceptability of the risks of those treatments, and beliefs about cancer, among others. The benefit-risk balance will differ widely among patients because a potential net benefit in reducing the risk of prostate cancer death for some men must be balanced against the risk of potentially serious or even life-threatening harms. In addition, the willingness of different patients to accept different risks varies. It is also now recognized that the increased uptake of active surveillance by men with a low-risk prostate cancer might mitigate the harms of over-diagnosis. Accordingly, the results of the Atellica IM fPSAII are only one of many other factors that will be taken into consideration in shared decision-making. In this clinical setting, where there are many unknowns with respect to the likelihood of a diagnosis of prostate cancer, and the likely behavior of such a cancer should it be diagnosed, this test is judged to have an acceptable benefit-risk profile.

Patient Perspectives:

This submission either did not include specific information on patient perspectives, or, the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The data from the analytical performance and clinical performance studies support the safety and effectiveness of the Atellica IM fPSAII as an aid in discriminating between prostate cancer and benign prostatic disease in men aged 50 years and older with total prostate-specific antigen (tPSA) values between 4 ng/mL and 10 ng/mL measured by the Atellica IM tPSAII, and a digital rectal examination (DRE) nonsuspicious for cancer

XV. CDRH DECISION

CDRH issued an approval order on May 11, 2026.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820), which was in effect at the time of the inspection. As of February 2, 2026, the revised part 820, referred to as the Quality Management System Regulation (QMSR), is effective.

XVI. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVII. REFERENCES

Not applicable.