SIEMENS Healthineers

Prostate-Specific Antigen (PSA)

Current Revision and Date[a]	Rev. 05, 2022-10	
Product Name	Atellica IM Prostate-Specific Antigen (PSA)	REF 10995662 (100 tests)
		REF 10995663 (500 tests)
Abbreviated Product Name	Atellica IM PSA	
Test Name/ID	PSA	
Systems	Atellica IM Analyzer	
Materials Required but Not Provided	Atellica IM CAL Q	REF 10995517 (2-pack)
		REF 10995518 (6-pack)
	Atellica IM APW1	REF 10995458
Optional Materials	Atellica IM Multi-Diluent 2	REF 10995644
	Atellica IM PSA MCM	REF 10995664
Specimen Types	Serum	
Sample Volume	35 µL	
Measuring Interval	0.01–100.00 ng/mL (µg/L)	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

CE 0197

WARNING

The concentration of total PSA in a given specimen, as determined by assays from different manufacturers, can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the assay for total PSA used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining serial levels of total PSA is changed, the laboratory must perform additional testing to confirm baseline values.

Intended Use

The Atellica® IM Prostate-Specific Antigen (PSA) assay is for *in vitro* diagnostic use in the quantitative measurement of prostate-specific antigen in human serum using the Atellica® IM Analyzer.

This assay is indicated for the measurement of serum PSA, in conjunction with a digital rectal exam (DRE), as an aid in the detection of prostate cancer in men aged 50 years and older. This assay is further indicated as an aid in the management (monitoring) of patients with prostate cancer.

Summary and Explanation

Prostate-specific antigen (PSA) is a single-chain glycoprotein normally found in the cytoplasm of the epithelial cells lining the acini and ducts of the prostate gland.[1] PSA is a neutral serine protease of 240 amino acids involved in the lysis of seminal coagulum.[2,3]

PSA is detected in the serum of males with normal, benign hypertrophic, and malignant prostate tissue. PSA is not detected in the serum of males without prostate tissue (because of radical prostatectomy or cystoprostatectomy) or in the serum of most females. The fact that PSA is unique to prostate tissue makes it a suitable marker for monitoring men with cancer of the prostate. PSA is also useful for determining possible recurrence after therapy when used in conjunction with other diagnostic indices.[4,5]

Measurement of serum PSA levels is not recommended as a screening procedure for the diagnosis of cancer because elevated PSA levels also are observed in patients with benign prostatic hypertrophy. However, studies suggest that the measurement of PSA in conjunction with digital rectal exam (DRE) and ultrasound provide a better method of detecting prostate cancer than DRE alone.[6–8]

PSA levels increase in men with cancer of the prostate, and after radical prostatectomy, PSA levels routinely fall to the undetectable range.[4] If prostatic tissue remains after surgery or metastasis has occurred, PSA appears to be useful in detecting residual and early recurrence of tumor.[9,10] Therefore, serial PSA levels can help determine the success of prostatectomy and the need for further treatment, such as radiation, endocrine or chemotherapy, and can help in monitoring the effectiveness of therapy.[4,5,8,11]

Principles of the Procedure

The Atellica IM PSA assay is a 2-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of 2 antibodies. The first antibody, in the Lite Reagent, is a goat polyclonal anti-PSA antibody labeled with acridinium ester. The second antibody, in the Solid Phase, is a mouse monoclonal anti-PSA antibody, which is covalently coupled to paramagnetic particles.

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

Reagents

Material Description	Storage	Stability[a]
Atellica IM PSA ReadyPack® primary reagent pack **Lite Reagent** 10.0 mL/reagent pack Goat polyclonal anti-PSA antibody (~77 ng/mL) labeled with acridinium ester in buffered saline; preservatives **Solid Phase** 25.0 mL/reagent pack Mouse monoclonal anti-PSA antibody (~25 µg/mL) covalently coupled to paramagnetic particles in buffered saline; preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 28 days
Atellica IM Multi-Diluent 2 ReadyPack ancillary reagent pack[b] 10.0 mL/pack Goat serum; sodium azide (0.1%); preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 28 days
Atellica IM APW1 ReadyPack ancillary reagent pack[c] 25.0 mL/reagent pack 0.4 N sodium hydroxide	Unopened at 2–8°C Onboard	Until expiration date on product 14 days

[a] Refer to *Storage and Stability*.
[b] Refer to *Optional Materials*.
[c] Refer to *Materials Required but Not Provided*.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens-healthineers.com.

The summary of safety and performance for this *in vitro* diagnostic medical device is available to the public in the European database on medical devices (EUDAMED) when this database is available and the information has been uploaded by the Notified Body. The web address of the EUDAMED public website is: https://ec.europa.eu/tools/eudamed.

H290, H319, H315
P234, P264, P280, P337+P313, P390, P501

Warning!
May be corrosive to metals. Causes serious eye irritation. Causes skin irritation.
Keep only in original container. Wash hands thoroughly after handling. Wear protective gloves/protective clothing/eye protection/face protection. If eye irritation persists: Get medical advice/attention. Absorb spillage to prevent material damage. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: sodium hydroxide (Atellica IM APW1).

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Note For information about reagent preparation, refer to *Preparing the Reagents* in the *Procedure* section.

Storage and Stability

Store reagents in an upright position. Protect the product from heat and light sources. Unopened reagents are stable until the expiration date on the product when stored at 2–8°C.

Store Atellica IM Multi-Diluent 2 in an upright position. Unopened Atellica IM Multi-Diluent 2 is stable until the expiration date on the product when stored at 2–8°C.

Store Atellica IM APW1 in an upright position. Unopened Atellica IM APW1 is stable until the expiration date on the product when stored at 2–8°C.

Do not use products beyond the expiration date printed on the product labeling.

Onboard Stability

Reagents are stable onboard the system for 28 days. Discard reagents at the end of the onboard stability interval.

Atellica IM Multi-Diluent 2 is stable onboard the system for 28 days.

Atellica IM APW1 is stable onboard the system for 14 days.

Do not use products beyond the expiration date printed on the product labeling.

Specimen Collection and Handling

Serum is the recommended sample type for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[12]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[13]
- Follow the instructions provided with your specimen collection device for use and processing.[14]
- Allow blood specimens to clot completely before centrifugation.[15]
- Keep tubes capped at all times.[15]
- Do not use specimens that have been stored at room temperature for longer than 8 hours.
- Tightly cap and refrigerate specimens at 2–8°C if the assay is not completed within 8 hours.

Storing the Specimen

- Freeze samples at ≤ -20°C if the samples are not assayed within 48 hours.
- Freeze samples only 1 time and mix thoroughly after thawing.

The handling and storage information provided here is based on data or references maintained by the manufacturer. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

Preparing the Samples

This assay requires 35 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For information about determining the minimum required volume, refer to the online help.

The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. Refer to *Dilutions*.

Note Do not use specimens with apparent contamination.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[15]

Note For a complete list of appropriate sample containers, refer to the online help.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10995662	1 ReadyPack primary reagent pack containing Atellica IM PSA Lite Reagent and Solid Phase Atellica IM PSA master curve and test definition MC TDEF	100
10995663	5 ReadyPack primary reagent packs containing Atellica IM PSA Lite Reagent and Solid Phase Atellica IM PSA master curve and test definition MC TDEF	500

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

REF	Description	
	Atellica IM Analyzer[a]	
10995517	Atellica IM CAL Q (calibrator)	2 x 2.0 mL low calibrator CAL L 2 x 2.0 mL high calibrator CAL H Calibrator lot-specific value sheet CAL LOT VAL

REF	Description	
10995518	Atellica IM CAL Q (calibrator)	6 x 2.0 mL low calibrator CAL L 6 x 2.0 mL high calibrator CAL H Calibrator lot-specific value sheet CAL LOT VAL
10995458	Atellica IM APW1 (probe wash)	2 ReadyPack ancillary reagent packs containing 25.0 mL/pack WASH

[a] Additional system fluids are required to operate the system: Atellica IM Wash, Atellica IM Acid, Atellica IM Base, and Atellica IM Cleaner. For system fluid instructions for use, refer to the Document Library.

Optional Materials

The following materials may be used to perform this assay, but are not provided:

REF	Description	
10995644	Atellica IM Multi-Diluent 2 (diluent)	2 ReadyPack ancillary reagent packs containing 10.0 mL/pack DIL
10995664	Atellica IM PSA MCM (master curve material)	9 x 1.0 mL levels of master curve material MCM

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 35 µL of sample into a cuvette.
2. Dispenses 250 µL of Solid Phase and 100 µL of Lite Reagent, then incubates the mixture for 8 minutes at 37°C.
3. Separates, aspirates, then washes the cuvette with special reagent water.

   Note For information about special reagent water requirements, refer to the online help.
4. Dispenses 300 µL each of Atellica IM Acid and Atellica IM Base to initiate the chemiluminescent reaction.
5. Reports results.

Preparing the Reagents

All reagents are liquid and ready to use. Before loading primary reagent packs onto the system, mix them by hand and visually inspect the bottom of the reagent pack to ensure that all particles are resuspended. For information about preparing the reagents for use, refer to the online help.

Preparing the System

Ensure that the system has sufficient reagent packs loaded in the reagent compartment. The system automatically mixes reagent packs to maintain homogeneous suspension of the reagents. For information about loading reagent packs, refer to the online help.

For automated dilutions, ensure that Atellica IM Multi-Diluent 2 is loaded on the system.

Master Curve Definition

Before initiating calibration on each new lot of reagent, load the assay master curve and test definition values by scanning the MC TDEF 2D barcodes. For loading instructions, refer to the online help.

Performing Calibration

For calibration of the Atellica IM PSA assay, use the Atellica IM CAL Q. Use the calibrators in accordance with the calibrator instructions for use.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- When changing lot numbers of primary reagent packs.
- At the end of the lot calibration interval, for a specified lot of calibrated reagent on the system.
- At the end of the pack calibration interval, for calibrated reagent packs on the system.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

At the end of the onboard stability interval, replace the reagent pack on the system with a new reagent pack. Recalibration is not required, unless the lot calibration interval is exceeded.

Stability Interval	Days
Lot Calibration	29
Pack Calibration	28
Reagent Onboard Stability	28

For information about lot calibration and pack calibration intervals, refer to the online help.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Performing Quality Control

For quality control of the Atellica IM PSA assay, use an appropriate quality control material of known analyte concentration with at least 2 levels (low and high) at least once during each day that samples are analyzed. For assistance in identifying a quality control material, refer to *Atellica® IM Quality Control Material Supplement* available on siemens-healthineers.com.

Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

- Following a valid calibration
- With use of a new lot of reagent
- When troubleshooting test results that do not match clinical conditions or symptoms

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the system online help.

Taking Corrective Action

If the quality control results do not fall within the assigned values, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the online help.

Results

Calculation of Results

The system determines the result using the calculation scheme described in the online help. The system reports results in ng/mL (common units) or µg/L (SI units), depending on the units defined when setting up the assay.

Conversion formula: 1 ng/mL (common units) = 1 µg/L (SI units).

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Dilutions

The assay measuring interval for serum is 0.01–100.00 ng/mL (µg/L). For information about dilution options, refer to the online help.

Serum samples with total PSA levels > 100.00 ng/mL (µg/L) must be diluted and retested to obtain accurate results

For automated dilutions, ensure that Atellica IM Multi-Diluent 2 is loaded on the system. Ensure that sufficient sample volume is available to perform the dilution and that the appropriate dilution factor is selected when scheduling the test, as indicated in the table below. Enter the dilution setpoint ≤ 100.00 ng/mL (µg/L).

Sample	Dilution	Sample Volume (µL)
Serum	1:2	75
Serum	1:5	30
Serum	1:10	40
Serum	1:50	40
Serum	1:100	40

Interpretation of Results

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

Limitations

The following information pertains to limitations of the assay:

WARNING

Do not predict disease recurrence solely on serial PSA values.

Note

Do not interpret levels of PSA as absolute evidence of the presence or the absence of malignant disease. Before treatment, patients with confirmed prostate carcinoma frequently have levels of PSA within the range observed in healthy individuals. Elevated levels of PSA can be observed in patients with nonmalignant diseases. Measurements of PSA should always be used in conjunction with other diagnostic procedures, including information from the patient's clinical evaluation.

The concentration of total PSA in a given specimen determined with assays from different manufacturers can vary due to differences in assay methods, calibration, and reagent specificity. Total PSA determined with different manufacturers' assays will vary depending on the method of standardization and antibody specificity.

- The Atellica IM PSA assay is intended to be used as an aid in the detection of prostate cancer and as an aid in the management (monitoring) of prostate cancer patients, in accordance with current clinical practice guidelines. These guidelines define biochemical recurrence of prostate cancer as a detectable or rising PSA value post-radical prostatectomy that is ≥ 0.20 ng/mL (µg/L) with a second confirmatory level of ≥ 0.20 ng/mL (µg/L), thus use of PSA values < 0.20 ng/mL (µg/L) is not recommended to identify patients at risk of biochemical recurrence of prostate cancer.[16,17]
- Specimens obtained from patients undergoing prostate manipulation, especially needle biopsy and transurethral resection, may show erroneously high results.[6] Care should be taken that PSA samples are drawn before these procedures are performed.
- Prostate cancer patients under treatment with anti-androgens and LHRH agonists may exhibit markedly reduced levels of PSA.[18,19] Also, men treated for benign prostatic hyperplasia with inhibitors of 5α-reductase (finasteride) may demonstrate a significant reduction in PSA levels compared to values prior to treatment.[20] Care should be taken when interpreting values from these individuals.
- The concentration of PSA in a given specimen determined with assays from different manufacturers can vary because of differences in assay methods, calibration, and reagent specificity.[21] PSA in serum and in seminal fluid exists primarily in complexed and free forms, respectively.[22] Quality control samples may be produced by introducing seminal fluid PSA into serum matrices. PSA 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.
- Patient samples may contain heterophilic antibodies that could react in immunoassays to give falsely elevated or depressed results. This assay is designed to minimize interference from heterophilic antibodies.[23,24]

Expected Values

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ACS:180™ system. Expected values were established using the ACS:180 system.

To confirm the distribution of total PSA in patients, as shown below, serum samples from healthy subjects and patients with various malignant diseases were analyzed. The patients included in this study represent a variety of disease states, from active, progressive malignancy to no clinical evidence of disease. The frequency of positive PSA results is significantly lower in patients with no evidence of active disease compared to those with active disease.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.[25] Consider these values as guidance only.

% Distribution of PSA by Diagnostic Category						
Patient Diagnosis	**N[a]**	**0.0–4.0 ng/mL (µg/L)**	**4.1–10 ng/mL (µg/L)**	**10.1–40 ng/mL (µg/L)**	**> 40 ng/mL (µg/L)**	**Median PSA ng/mL (µg/L)**
Apparently Healthy						
Female	100	100.0	0.0	0.0	0.0	< 0.06
Male < 40	71	100.0	0.0	0.0	0.0	0.73
Male 40–50	50	100.0	0.0	0.0	0.0	0.53
Male 50–60	54	100.0	0.0	0.0	0.0	0.61
Male 60–70	50	100.0	0.0	0.0	0.0	0.85
Male > 70	58	100.0	0.0	0.0	0.0	0.77
Total Males	283	100.0	0.0	0.0	0.0	0.71
Prostate Cancer						
Stage A	42	69.0	26.2	4.8	0.0	3.92
Stage B	50	60.0	32.0	8.0	0.0	3.52
Stage C	43	20.9	72.1	4.7	2.3	5.25
Stage D	46[b]	56.5	21.7	19.6	2.2	3.48
Total Prostate	191	51.6	38.0	9.3	1.1	4.04
Benign Diseases						
Prostate Hypertrophy (BPH)	152	46.7	32.9	20.4	0.0	4.37
Genitourinary (GU)	50	90.0	8.0	2.0	0.0	1.38
Prostatitis	18	27.8	5.6	5.6	61.1	125.9
Rheumatoid Factor	5	100.0	0.0	0.0	0.0	0.58
Other Cancers						
Breast	10	100.0	0.0	0.0	0.0	0.08
Renal	6	100.0	0.0	0.0	0.0	0.37
Pulmonary	10	100.0	0.0	0.0	0.0	0.08
Misc. GU	39	92.3	5.1	2.6	0.0	0.42
Gastrointestinal	12	91.7	0.0	0.0	8.3	0.90
Other	18	100.0	0.0	0.0	0.0	0.45

[a] Number of samples tested.
[b] Includes sera from treated patients

Expected Values in the Detection of Prostate Cancer

An evaluation was conducted to test the effectiveness of PSA along with DRE as an aid in detection of prostate cancer. A total of 291 biopsied men aged 50 years or older were included in the study. In the population of 291 subjects, 76 men or 26.1% were found to have cancer. The positive predictive value (PPV) of PSA at the cut-off value of 4.0 ng/mL (µg/L) was 28.4%. This study also demonstrated that PSA testing, when used in conjunction with DRE, was more effective than DRE alone.

PSA elevations > 4.0 ng/mL (µg/L) may warrant additional testing, even if the DRE is negative. However, the converse is also true: a subject with suspicious DRE and normal PSA may also require additional testing since DRE detected 17% (13/76) of cancers that PSA determinations did not.

Refer to the following table for a summary of the study results:

ACS:180 PSA	Number of Subjects	Number of Cancers	% Positive Biopsies
All subjects	291	76	26.1
PSA > 4.0 ng/mL (µg/L) DRE+	218 127	62 55	28.4 43.3
PSA < 4.0 ng/mL (µg/L), DRE- PSA > 4.0 ng/mL (µg/L), DRE-	32 132	1 20	3.1 15.2
PSA < 4.0 ng/mL (µg/L), DRE+ PSA > 4.0 ng/mL (µg/L), DRE+	41 86	13 42	31.7 48.8

DRE+ = Suspicious for cancer
DRE- = Not suspicious for cancer

Performance Characteristics

The reagent formulations used on the Atellica IM Analyzer are the same as those used on the ADVIA Centaur® and ACS:180 systems. Some performance characteristics for the Atellica IM assay were established using the ADVIA Centaur or ACS:180 systems.

Measuring Interval

The Atellica IM PSA assay provides results from 0.01–100.00 ng/mL (µg/L). The lower end of the measuring interval is defined by the analytical sensitivity. Report results below the measuring interval as < 0.01 ng/mL (µg/L). When sample results exceed the measuring interval, refer to *Dilutions*.

Specificity

There are no known cross-reactants for this assay.

Equimolar-response PSA assays recognize both forms of immunodetectable PSA, both free PSA and PSA-ACT, equally.[26] The antibodies used in the ADVIA Centaur PSA assay recognize free PSA and PSA-ACT on an equimolar basis in the range of 10–50% free PSA/total PSA which is representative of men with prostate cancer, no disease, and benign prostate hyperplasia.[27]

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[28] The assay is designed to have an analytical sensitivity of ≤ 0.01 ng/mL (µg/L), a limit of blank (LoB) ≤ 0.01 ng/mL (µg/L), a limit of detection (LoD) ≤ 0.03 ng/mL (µg/L), and a limit of quantitation (LoQ) ≤ 0.10 ng/mL (µg/L).

Representative detection capability data are shown below. Assay results obtained at individual laboratories may vary from the data presented.

Analytical sensitivity is defined as the concentration of PSA that corresponds to the RLUs that are 2 standard deviations more than the mean RLUs of 20 replicate determinations of the PSA zero standard. This response is an estimate of the minimum detectable concentration with 95% confidence. The analytical sensitivity for the Atellica IM PSA assay is 0.01 ng/mL (µg/L).

The LoB corresponds to the highest measurement result that is likely to be observed for a blank sample. The LoB of the Atellica IM PSA assay is 0.01 ng/mL (µg/L).

The LoD corresponds to the lowest concentration of PSA that can be detected with a probability of 95%. The LoD for the Atellica IM PSA assay is 0.02 ng/mL (µg/L), and was determined using 284 determinations with 120 blank and 164 low-level replicates, and an LoB of 0.01 ng/mL (µg/L).

The LoQ corresponds to the lowest amount of PSA in a sample at which the within-laboratory CV is ≤ 20%. The LoQ of the Atellica IM PSA assay is 0.02 ng/mL (µg/L), and was determined using multiple patient samples in the interval 0.002–0.181 ng/mL (µg/L). All samples were assayed in duplicate in each of 2 runs using 2 reagent lots, over a period of 20 days.

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[29] Samples were assayed on an Atellica IM Analyzer in duplicate in 2 runs per day for 20 days. The assay was designed to have within-laboratory precision of ≤ 0.03 SD for samples ≤ 0.11 ng/mL, ≤ 20.0% CV for samples from 0.11–0.90 ng/mL, ≤ 8.0% CV for samples from 1.00–20.00 ng/mL, and ≤ 10.0% CV for samples > 20.00 ng/mL. The following results were obtained:

			Repeatability		Within-Laboratory Precision	
Sample Type	N[a]	Mean ng/mL (µg/L)	SD[b] ng/mL (µg/L)	CV[c] (%)	SD ng/mL (µg/L)	CV (%)
Serum A	80	0.06	0.00	6.2	0.01	8.5
Serum B	80	0.32	0.01	2.1	0.01	3.2
Serum C	80	2.18	0.04	1.8	0.05	2.4
Serum D	80	4.76	0.07	1.6	0.10	2.2
Serum E	80	10.76	0.19	1.7	0.25	2.3
Serum F	80	19.63	0.35	1.8	0.54	2.8
Serum G	80	78.67	1.71	2.2	3.11	4.0
Control 1	80	0.60	0.01	2.0	0.02	3.2

			Repeatability		Within-Laboratory Precision	
Sample Type	**N[a]**	**Mean ng/mL (µg/L)**	**SD[b] ng/mL (µg/L)**	**CV[c] (%)**	**SD ng/mL (µg/L)**	**CV (%)**
Control 2	80	2.76	0.04	1.6	0.08	2.9
Control 3	80	16.56	0.26	1.6	0.45	2.7

[a] Number of samples tested.
[b] Standard deviation.
[c] Coefficient of variation.

Based on internal testing on the Atellica IM Analyzer, the overall reproducibility is estimated to be ≤ 10% CV or ≤ 0.03 ng/mL SD for samples tested and includes multiple reagent lots, instruments, days, and replicates. Performance of the assay at individual laboratories may vary.

Assay Comparison

The Atellica IM PSA assay is designed to have a correlation coefficient of ≥ 0.98 and a slope of 1.0 ±0.10 compared to the ADVIA Centaur PSA assay. Assay comparison was determined using the weighted Deming linear regression model in accordance with CLSI Document EP09-A3.[30] The following results were obtained:

Specimen	**Comparative Assay (x)**	**Regression Equation**	**Sample Interval**	**N[a]**	**r[b]**
Serum	ADVIA Centaur PSA	y = 0.93x + 0.238 ng/mL (µg/L)	3.10–66.79 ng/mL (µg/L)	105	0.996

[a] Number of samples tested.
[b] Correlation coefficient.

For 661 serum samples in the range of 0.07 –93.3 ng/mL (µg/L), the relationship between the ADVIA Centaur PSA assay to the ACS:180 PSA assay is described using ordinary least squares regression by the following equation:

Specimen	**Comparative Assay (x)**	**Regression Equation**	**Sample Interval**	**N[a]**	**r[b]**
Serum	ACS:180 PSA	y = 0.99x - 0.09 ng/mL (µg/L)	0.07–93.3 ng/mL (µg/L)	661	0.99

[a] Number of samples tested.
[b] Correlation coefficient.

Agreement of the assays may vary depending on the study design, comparative assay, and sample population used. Assay results obtained at individual laboratories may vary from the data presented.

Interferences

Interference testing was performed in accordance with CLSI Document EP7-A2.[31]

The following substances do not interfere with the Atellica IM PSA assay when present in serum at the concentrations indicated in the table below.

The potential interference of chemotherapeutic agents, therapeutic drugs, and tumor marker antigens was tested by adding these substances to serum pools containing PSA ranging from 0.77–7.12 ng/mL (µg/L). The level of PSA in each of these pools was then determined using the ADVIA Centaur PSA assay and normalized to the level without the respective drugs or antigen.

Substance	Substance Test Concentration (µg/mL)	Mean % Recovery (Spike/control x 100)
Cyclophosphamide	700	100.5
Doxorubicin hydrochloride	51.8	100
Methotrexate	22.72	101
Megestrol acetate	39.6	101
Diethylstilbestrol	5.0	100
Leuprolide (LUPRON)	15.0	100
Estramustine phosphate	81.7	99
Flutamide	10.0	100
Zoladex (Goserelin acetate)	7.2	98
Trypsin proscar (Finasteride)	0.37	102
Cardura	0.8	100

Hemolysis, Icterus, and Lipemia (HIL)

Serum specimens that are...	Demonstrate ≤ 5% change in results up to...
hemolyzed	500 mg/dL of hemoglobin
icteric	40 mg/dL of bilirubin
lipemic	1000 mg/dL of triglycerides

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Dilution Recovery

Six human serum samples in the range of 41.90–85.36 ng/mL (µg/L) of total PSA were diluted 1:2, 1:4, and 1:8 with Multi-Diluent 2 and assayed for recovery and parallelism. The recoveries ranged from 94.4%–109.0% with a mean of 102.4%.

Sample	Dilution	Observed (ng/mL)	Expected (ng/mL)	Observed (µg/L)	Expected (µg/L)	Recovery %
1	—	41.90	—	41.90	—	—
	1:2	21.79	20.95	21.79	20.95	104.0
	1:4	11.13	10.48	11.13	10.48	106.2
	1:8	5.67	5.24	5.67	5.24	108.2
	Mean					106.1
2	—	71.44	—	71.44	—	—

Sample	Dilution	Observed (ng/mL)	Expected (ng/mL)	Observed (µg/L)	Expected (µg/L)	Recovery %
	1:2	38.22	35.72	38.22	35.72	107.0
	1:4	19.25	17.86	19.25	17.86	107.8
	1:8	9.30	8.93	9.30	8.93	104.1
	Mean					106.3
3	—	68.73	—	68.73	—	—
	1:2	33.41	34.37	33.41	34.37	97.2
	1:4	16.70	17.18	16.70	17.18	97.2
	1:8	8.29	8.59	8.29	8.59	96.5
	Mean					97.0
4	—	85.36	—	85.36	—	—
	1:2	43.32	42.68	43.32	42.68	101.5
	1:4	23.25	21.34	23.25	21.34	109.0
	1:8	11.62	10.67	11.62	10.67	108.9
	Mean					106.5
5	—	49.79	—	49.79	—	—
	1:2	24.63	24.90	24.63	24.90	98.9
	1:4	12.38	12.45	12.38	12.45	99.4
	1:8	6.33	6.22	6.33	6.22	101.8
	Mean					100.0
6	—	58.10	—	58.10	—	—
	1:2	27.42	29.05	27.42	29.05	94.4
	1:4	14.36	14.53	14.36	14.53	98.8
	1:8	7.38	7.26	7.38	7.26	101.7
	Mean					98.3
Mean						102.4

Results were established using the ADVIA Centaur system. Assay results obtained at individual laboratories may vary from the data presented.

Spiking Recovery

Varying amounts of PSA were added to 5 serum samples with endogenous PSA levels ranging from 0.81–3.05 ng/mL (µg/L). The amount of PSA that was added varied from 24.8–63.4 ng/mL (µg/L). When compared to the expected value, the measured (recovered) values of total PSA averaged 98.8% with a range of 92.6%–107.3%.

Sample	Amount Added (ng/mL)	Observed (ng/mL)	Amount Added (µg/L)	Observed (µg/L)	Recovery %
1	—	0.81	—	0.81	—
	24.8	25.39	24.8	25.39	99.1
	43.7	47.68	43.7	47.68	107.3
	63.4	61.31	63.4	61.31	95.4
	Mean				100.6
2	—	1.05	—	1.05	—
	24.8	24.66	24.8	24.66	95.2
	43.7	43.38	43.7	43.38	96.9
	63.4	59.73	63.4	59.73	92.6
	Mean				94.9
3	—	2.31	—	2.31	—
	24.8	27.51	24.8	27.51	101.6
	43.7	47.68	43.7	47.68	103.8
	63.4	61.31	63.4	61.31	93.1
	Mean				99.5
4	—	2.73	—	2.73	—
	24.8	26.90	24.8	26.90	97.5
	43.7	47.97	43.7	47.97	103.5
	63.4	66.13	63.4	66.13	100.0
	Mean				100.3
5	—	3.05	—	3.05	—
	24.8	27.81	24.8	27.81	99.8
	43.7	46.28	43.7	46.28	98.9
	63.4	64.74	63.4	64.74	97.3
	Mean				98.7
Mean					98.8

Results were established using the ACS:180 system. Assay results obtained at individual laboratories may vary from the data presented.

High-Dose Hook Effect

High total PSA concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with total PSA concentrations as high as 2,500 ng/mL (µg/L) will report > 100.00 ng/mL (µg/L).

Standardization

The Atellica IM PSA assay is traceable to an internal standard manufactured using highly purified material. Value assignment was based on adjustment to a reference method comparison protocol.[32] The assay standardization is traceable to World Health Organization (WHO) International Standard (96/670).

Assigned values for calibrators are traceable to this standardization.

Technical Assistance

According to EU regulation 2017/746, any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or patient is established.

For customer support, contact your local technical support provider or distributor.

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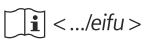
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Manufacturer	5.1.1[a]		Authorized representative in the European Community	5.1.2[a]
	Use-by date	5.1.4[a]		Authorized representative in Switzerland	Proprietary
	Catalog number	5.1.6[a]		Batch code	5.1.5[a]
	Consult Instructions for Use	5.4.3[a]		Contains sufficient for <n> tests	5.5.5[a]
	Internet URL address to access the electronic instructions for use	Proprietary		Version of Instructions for Use	Proprietary
	*In vitro* diagnostic medical device	5.5.1[a]		Revision	Proprietary
	Prescription device (US only)	FDA[b]		Unique Device Identifier	5.7.10[c]
	CE Marking with Notified Body	EU IVDR[d]		CE Marking	EU IVDR[d]
	Temperature limit	5.3.7[a]		Keep away from sunlight	5.3.2[a]
	Upper limit of temperature	5.3.6[a]		Lower limit of temperature	5.3.5[a]
	Do not re-use	5.4.2[a]		Do not freeze	Proprietary
	Recycle	1135[e]		This way up	0623[e]
	Biological risks	5.4.1[a]		Caution	5.4.4[a]
	Common Units	Proprietary		International System of Units	Proprietary
YYYY-MM-DD	Date format (year-month-day)	N/A	**YYYY-MM**	Date format (year-month)	N/A

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Document face up[f]	1952[e]		Handheld barcode scanner	Proprietary
	Target	Proprietary		Mixing of substances	5657[g]
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.	Proprietary		Interval	Proprietary
MATERIAL ID	Unique material identification number	Proprietary	MATERIAL	Material	Proprietary
CONTROL TYPE	Type of control	Proprietary	CONTROL NAME	Name of control	Proprietary
CONTROL LOT VAL	Quality control lot value	Proprietary	CAL LOT VAL	Calibrator lot value	Proprietary

[a] International Standard Organization (ISO). ISO 15223-1 Medical Devices- Symbols to be used with medical device labels, labelling and information to be supplied.
[b] Federal Register. Vol. 81, No 115. Wednesday, June 15, 2016. Rules and Regulations: 38911.
[c] ISO 15223-1:2020-04
[d] IVDR REGULATION (EU) 2017/746
[e] International Standard Organization (ISO). ISO 7000 Graphical symbols for use on equipment.
[f] Indicates Assay-eNote
[g] International Electrotechnical Commission (IEC). IEC 60417-1 Graphical symbols for use on equipment – Part 1: Overview and Application

Legal Information

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