SIEMENS Healthineers

total PSA II (tPSAII)

Current Revision and Date[a]	Rev. 01, 202X-XX	
Product Name	Atellica IM total PSA II (tPSAII)	REF 11202246 (100 tests) REF 11202247 (500 tests)
Abbreviated Product Name	Atellica IM tPSAII	
Test Name/ID	tPSAII	
Systems	Atellica IM Analyzer	
Optional Materials	Atellica IM Multi-Diluent 2	REF 10995644
	Atellica IM tPSAII Master Curve Material (tPSAII MCM)	REF 11202245
Specimen Types	Serum, EDTA plasma, lithium heparin plasma	
Sample Volume	30 µL	
Measuring Interval	0.009–50.000 ng/mL (µg/L)	

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

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.

Intended Use

The Atellica® IM total PSA II (tPSAII) assay is for *in vitro* diagnostic use in the quantitative measurement of total prostate-specific antigen (PSA) in human serum and plasma (EDTA and lithium heparin) using the Atellica® IM Analyzer.

This assay is indicated as an aid in the detection of prostate cancer in conjunction with a digital rectal exam (DRE) in men aged 50 years and older. Prostate biopsy is required for diagnosis of prostate cancer.

Summary and Explanation

PSA is a single-chain glycoprotein normally found in the cytoplasm of the epithelial cells that line 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.[4,5] 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.[4] The fact that PSA is unique to prostate tissue makes it a suitable marker for monitoring men with cancer of the prostate. PSA is useful for determining possible recurrence after therapy when used in conjunction with other diagnostic indices.[6]

Measurement of serum PSA levels alone is not recommended for systematic population screening as it has been associated with over-treatment of indolent cancers and under-treatment of metastatic cancers. However, targeted PSA testing based on age, race, hereditary or other risk factors, and life expectancy can help reduce the number of unnecessary biopsies while detecting potentially metastatic disease early enough to reduce mortality.[7-9]

PSA measurement with a DRE is also recommended to guide biopsy decision-making in symptomatic men. European and international urology, oncology, and geriatric oncology guidelines note, however, that PSA is a better univariate predictor of prostate cancer than either DRE or transrectal ultrasound.[7] Periodic PSA monitoring is used for active surveillance in men with biopsy-determined low-risk (indolent) localized tumors who do not undergo immediate therapy.[7]

Radical prostatectomy (RP) may be considered for low-, intermediate-, or high-risk and locally advanced prostate cancers. If RP successfully removes all prostate tissue, PSA levels routinely fall to the undetectable range.[8] If, however, prostatic tissue remains after surgery or metastasis has occurred, PSA monitoring can detect residual tissue as well as early recurrence of disease.[9-11]

European, international, and United States guidelines stress that a single PSA level might not be sufficient to establish prostate cancer recurrence. Therefore, serial PSA levels should be considered for determining the need for adjuvant or salvage radiation therapy, endocrine therapy, or chemotherapy, and for monitoring the effectiveness of therapy.[7-11]

Principles of the Procedure

This assay is a fully automated sandwich immunoassay using acridinium ester chemiluminescent technology. The assay uses 3 monoclonal mouse antibodies in the Atellica IM tPSAII 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 a monoclonal mouse anti-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.

Reagents

Material Description	Storage	Stability
tPSAII ReadyPack® primary reagent pack[a, b] **Lite Reagent** 10.0 mL/reagent pack Unlabeled monoclonal mouse anti-free-PSA (fPSA) antibody (~250 ng/mL); monoclonal mouse anti-PSA antibody (~180 ng/mL) labeled with acridinium ester; buffer; bovine serum albumin (BSA); preservative **Solid Phase** 20.0 mL/reagent pack Monoclonal mouse anti-PSA antibody (~3.5 µg/mL) labeled with biotin and bound to streptavidin paramagnetic particles; buffer; BSA, bovine gamma globulin (BGG); sodium azide (< 0.1%); preservative	Unopened at 2–8°C Onboard	Until expiration date on product 42 days
tPSAII CAL[a] 2.0 mL/vial Purified PSA from human seminal fluid in buffer; BSA; sodium azide (< 0.1%)	Unopened at 2–8°C Opened at 2–8°C On the system at room temperature	Until expiration date on product 30 days 8 hours
Atellica IM Multi-Diluent 2 ReadyPack ancillary reagent pack[c] 10.0 mL/pack Goat serum; sodium azide (0.1%); preservatives	Unopened at 2–8°C Onboard	Until expiration date on product 28 days

[a] Store in an upright position.
[b] Prevent exposure to light.
[c] Refer to *Optional Materials*

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.

H317, H411
P280, P273, P302+P352, P333+P313, P362+P364, P391, P501

Warning!
May cause an allergic skin reaction. Toxic to aquatic life with long lasting effects.
Wear protective gloves/protective clothing/eye protection/face protection. Avoid release to the environment. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Take off contaminated clothing and wash it before reuse. Collect spillage. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: Reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1) (tPSAII CAL)

H412	Harmful to aquatic life with long lasting effects.
P273, P501	Avoid release to the environment. Dispose of contents and container in accordance with all local, regional, and national regulations. **Contains:** 4-Nonylphenol, branched, ethoxylated (tPSAII Lite Reagent)

Warning! Potential Biohazard

Contains human source material.

No known test method can ensure that products derived from human source materials will not transmit infection. These materials should be handled using good laboratory practices and universal precautions.[12-14]

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.

Storage and Stability

Store all reagents in an upright position, away from light. Do not use products beyond the expiration date printed on the product labeling or beyond the in-use stability interval.

For information about product storage and stability, refer to *Reagents*.

Specimen Collection and Handling

Serum and plasma (EDTA and lithium heparin) are the recommended specimen types for this assay.

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.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[14]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[15]
- Follow the instructions provided with your specimen collection device for use and processing.[16]
- Allow blood specimens to clot completely before centrifugation.[17]
- Keep tubes capped at all times.[17]

Storing the Specimen

- After centrifugation, specimens in the primary collection device are stable for up to 24 hours at 2–8°C. Samples in the primary collection device include serum stored on the clot, plasma stored on packed red cells, and samples processed and stored in gel-barrier blood collection tubes.
- Separated samples are stable for up to 8 hours at room temperature, and for up to 3 days at 2–8°C.
- Separated samples are stable at ≤ -80°C for up to 15 months. Avoid more than 4 freeze-thaw cycles. Do not store in a frost-free freezer. Thoroughly mix thawed samples and centrifuge them before using.

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 30 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 a complete list of appropriate sample containers and information about determining the minimum required volume, refer to the system online help.

Do not use samples with apparent contamination.

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

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

Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[17]

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
11202246	1 ReadyPack primary reagent pack containing tPSAII Lite Reagent and Solid Phase Atellica IM tPSAII master curve and test definition MC TDEF 1 vial tPSAII CAL low calibrator CAL L 1 vial tPSAII CAL high calibrator CAL H Atellica IM tPSAII CAL calibrator assigned value sheet CAL LOT VAL	100
11202247	5 ReadyPack primary reagent packs containing tPSAII Lite Reagent and Solid Phase Atellica IM tPSAII master curve and test definition MC TDEF 2 vials tPSAII CAL low calibrator CAL L 2 vials tPSAII CAL high calibrator CAL H Atellica IM tPSAII CAL calibrator assigned value sheet CAL LOT VAL	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]

[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) DIL
11202245	Atellica IM tPSAII MCM (master curve material) MCM

Assay Procedure

The system automatically performs the following steps:

1. Dispenses 30 µL of sample into a cuvette.
2. Dispenses 200 µL of Solid Phase and 100 µL of Lite Reagent, then incubates for 8 minutes at 37°C.
3. Performs a wash sequence using Atellica IM Wash.
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 the packs onto the system, reagents require mixing. For information about mixing the reagents, refer to the system online help.

Preparing the System

Ensure that sufficient materials are loaded on the system. Refer to *Materials Provided* and *Optional Materials* for guidance about required reagents.

For information about loading products, refer to the system online help.

Master Curve Definition

Before initiating calibration on each new lot of reagent, enter the assay master curve and test definition by scanning the MC TDEF 2D barcodes. For information about entering the master curve and test definition, refer to the system online help.

Performing Calibration

For calibration of the assay, use the calibrators provided with each kit.

Note Calibrators provided in an assay kit must only be used with the reagent lot provided in the same kit.

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.

Note When loading a new primary reagent pack, a calibration is not required if there is a valid lot calibration. For information about lot calibration and pack calibration, refer to the system online help.

Stability Interval	Days
Lot Calibration	42
Pack Calibration	14
Reagent Onboard Stability	42

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

Preparing the Calibrators

Calibrators are liquid and ready to use. Allow materials to equilibrate to room temperature. Gently mix and invert the vials to ensure homogeneity of the material. Each dispensed drop is approximately 50 µL.

Use within the stability limits specified in *Reagents* and discard any remaining material.

Calibration Procedure

The required sample volume for testing depends on several factors. For information about sample volume requirements, refer to the system online help.

Use the following lot-specific materials to perform calibration:

- For the master curve and assay test definitions, refer to the lot-specific master curve and test definition sheet MC TDEF provided with the assay reagents.
- Calibrators provided in an assay kit must only be used with reagents from that assay kit lot. Do not use calibrators from one assay kit lot with reagents from a different assay kit lot.
- For the calibrator definitions, refer to the calibrator assigned value sheet CAL LOT VAL provided with the calibrator materials.
- Generate lot-specific barcode labels to use with the calibrator samples.

For instructions about how to perform the calibration procedure, refer to the system online help.

Performing Quality Control

For quality control of the assay, use appropriate quality control material with a minimum of two levels (low and high) at least once every 24 hours 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.

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.

Taking Corrective Action

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

Results

Calculation of Results

The system determines the result using the calculation procedure described in the system 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 = 1 µg/L

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

Interpretation of Results

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.

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:

- Results obtained with the assay may not be used interchangeably with values obtained with different manufacturers' assay methods.
- Specimens obtained from patients undergoing prostate manipulation, especially needle biopsy and transurethral resection, may show erroneously high results. Care should be taken that PSA samples are drawn before these procedures are performed.

- 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.
- Patient samples may contain heterophilic antibodies that could react in immunoassays and cause falsely elevated or depressed results.[23,24] This assay is designed to minimize interference from heterophilic antibodies. Additional information, such as the patient's medical history and clinical presentation should be considered in conjunction with the test result.

Reference Interval and Expected Values

To evaluate the distribution of total PSA in male patients, as shown below, serum samples from healthy subjects and patients with various prostate diseases were analyzed using the Atellica IM Analyzer. 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 (≥ 4 ng/mL [µg/L]) is significantly lower in patients with no evidence of active disease compared to those with active disease.

	N	<4 ng/mL (%)	4–10 ng/mL (%)	>10–30 ng/mL (%)	>30–50 ng/mL (%)	>50 ng/mL (%)	Median (ng/mL)	95th Percentile
Apparently Healthy								
50–59 years	294	95.2	4.4	0.3	0.0	0.0	0.896	3.942
60–69 years	293	92.5	6.8	0.0	0.3	0.3	1.153	4.764
70–99 years	140	87.1	12.1	0.7	0.0	0.0	1.596	6.607

	N	<4 ng/mL (%)	4–10 ng/mL (%)	>10–30 ng/mL (%)	>30–50 ng/mL (%)	>50 ng/mL (%)	Median (ng/mL)
Prostate Cancer							
Gleason 6	442	18.2	70.4	10.0	0.9	0.2	5.806
Gleason 7+	1075	8.4	58.0	24.7	3.4	5.5	7.576
Total Prostate Cancer	1517	11.3	61.6	20.4	2.7	4.0	6.985

	N	<4 ng/mL (%)	4–10 ng/mL (%)	>10–30 ng/mL (%)	>30–50 ng/mL (%)	>50 ng/mL (%)	Median (ng/mL)
Benign Diseases							
Benign Prostatic Hyperplasia (BPH)	32	21.9	62.5	15.6	0.0	0.0	5.740
Prostatic Intraepi-thelial Neoplasia (PIN)	93	17.3	67.3	13.3	1.0	1.0	5.800

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.

Detection of Prostate Cancer

A clinical performance study was conducted to support the Atellica IM tPSAII assay as an aid in detection of prostate cancer in conjunction with DRE. Samples were collected from men aged 50 years and older who had been referred to a urologist for evaluation of the presence of prostate cancer at 25 clinical sites across the United States. Results were established using the Atellica IM Analyzer. All subjects underwent a biopsy. Therefore, the clinical performance data may not fully reflect the broader population, as men who did not have a biopsy were not included in the evaluation. In the population of 2582 subjects, 1517 men (58.8%) were found to have cancer. Data from the clinical performance study is presented below.

Positive Biopsy (prostate cancer present)				**Negative Biopsy (no prostate cancer present)**			
	DRE +	**DRE -**	**Total**		**DRE +**	**DRE -**	**Total**
tPSAII ≥ 4.0 ng/mL	431	914	1345	**tPSAII ≥ 4.0 ng/mL**	117	681	798
tPSAII < 4.0 ng/mL	51	121	172	**tPSAII < 4.0 ng/mL**	72	195	267
Total	482	1035	1517	**Total**	189	876	1065

PSA elevations ≥ 4.0 ng/mL (µg/L) may warrant additional testing, even if the DRE is negative. Of the 1517 men with prostate cancer, 914 (60.2%) had a negative DRE and tPSAII ≥ 4.0 ng/mL (µg/L). A subject with suspicious DRE and normal PSA levels ≥ 4.0 ng/mL (µg/L) may also require additional testing. Of the 1517 men with prostate cancer, 51 (3.4%) had a positive DRE and tPSAII < 4.0 ng/mL (µg/L). The distributions of DRE and Atellica IM tPSAII results among men with and without prostate cancer are presented below.

	Biopsy Result				
Category	**Positive**	**Negative**	**Total**	**% of Subjects with Positive Biopsy Within Category**	**Sensitivity of Category**
DRE+	482	189	671	71.8% (482/671)	31.8% (482/1517)
DRE-	1035	876	1911	54.2% (1035/1911)	68.2% (1035/1517)
tPSAII ≥ 4.0 ng/mL, DRE+	431	117	548	78.6% (431%/548)	28.4% (431/1517)
tPSAII ≥ 4.0 ng/mL, DRE-	914	681	1595	57.3% (914/1595)	60.2% (914/1517)
tPSAII < 4.0 ng/mL, DRE+	51	72	123	41.5% (51/123)	3.4% (51/1517)
tPSAII < 4.0 ng/mL, DRE-	121	195	316	38.3% (121/316)	8.0% (121/1517)
All subjects	1517	1065	2582	58.8% (1517/2582)	100% (1517/1517)

Measuring Interval

The analytical measuring interval is 0.009–50.000 ng/mL (µg/L)

The lower limit of the measuring interval is defined by the limit of quantitation (LoQ). Report results below the measuring interval as < 0.009 ng/mL (µg/L).

Detection Capability

Limit of Blank (LoB)	0.004 ng/mL (µg/L)
Limit of Detection (LoD)	0.006 ng/mL (µg/L)
Limit of Quantitation (LoQ)	0.009 ng/mL (µg/L)

Detection capability was determined in accordance with CLSI Document EP17-A2.[26]

The LoB corresponds to the highest measurement result likely to be observed for a blank sample with a probability of 95%.

The LoD corresponds to the lowest analyte concentration that can be detected with a probability of 95%.

The LoQ corresponds to the lowest analyte concentration at which the within laboratory CV is ≤ 15.0%.

Precision

Precision was determined using the Atellica IM Analyzer in accordance with CLSI Document EP05-A3.[27] Samples were assayed in replicates of 2 with 2 runs per day using a 20-day protocol. The following results are representative of the performance of the assay:

			Repeatability		Within-Laboratory Precision	
Sample	**N[a]**	**Mean ng/mL (µg/L)**	**SD[b] ng/mL (µg/L)**	**CV[c] (%)**	**SD ng/mL (µg/L)**	**CV (%)**
Serum A	80	0.024	0.0012	5.0	0.0015	6.4
Serum B	80	0.214	0.0046	2.1	0.0054	2.5
Serum C	80	3.718	0.0623	1.7	0.0847	2.3
Serum D	80	10.196	0.1739	1.7	0.2714	2.7
Serum E	80	19.768	0.3270	1.7	0.4612	2.3
Serum F	80	38.232	0.5632	1.5	1.0700	2.8
Control 1	80	0.152	0.0030	2.0	0.0038	2.5
Control 2	80	4.463	0.0608	1.4	0.1170	2.6
Control 3	80	19.853	0.2951	1.5	0.5045	2.5

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

Reproducibility

Reproducibility was determined using the Atellica IM Analyzer in accordance with CLSI Document EP05-A3.[27] Testing was performed using 3 sites and 3 reagent lots. Samples were assayed in replicates of 3 with 2 runs per day using a 5-day protocol (Number of measurements per sample = 270). The following results are representative of the performance of the assay:

		Repeatability		Between Run		Between Day		Between Lot		Between Site		Repro-ducibility	
Sample	**Mean ng/mL (µg/L)**	**SD[a] ng/mL (µg/L)**	**CV[b] (%)**	**SD ng/mL (µg/L)**	**CV (%)**	**SD ng/mL (µg/L)**	**CV (%)**	**SD ng/mL (µg/L)**	**CV (%)**	**SD ng/mL (µg/L)**	**CV (%)**	**SD ng/mL (µg/L)**	**CV (%)**
Serum A	0.102	0.0017	1.7	0.0016	1.6	0.0005	0.5	0.0011	1.1	0.0015	1.5	0.0030	2.9
Serum B	2.061	0.0303	1.5	0.0212	1.0	0.0144	0.7	0.0378	1.8	0.0261	1.3	0.0607	2.9
Serum C	4.201	0.0624	1.5	0.0281	0.7	0.0188	0.4	0.0582	1.4	0.0625	1.5	0.1111	2.6
Serum D	10.304	0.1531	1.5	0.1451	1.4	0.0000	0.0	0.1186	1.2	0.1187	1.2	0.2696	2.6
Serum E	20.248	0.2963	1.5	0.2648	1.3	0.0850	0.4	0.1297	0.6	0.5816	2.9	0.7213	3.6
Serum F	42.673	0.7532	1.8	0.4541	1.1	0.2790	0.7	0.0000	0.0	1.1665	2.7	1.4873	3.5
Control 1	0.178	0.0031	1.7	0.0034	1.9	0.0000	0.0	0.0018	1.0	0.0043	2.4	0.0066	3.7

Sample	Mean ng/mL (µg/L)	Repeatability SD[a] ng/mL (µg/L)	Repeatability CV[b] (%)	Between Run SD ng/mL (µg/L)	Between Run CV (%)	Between Day SD ng/mL (µg/L)	Between Day CV (%)	Between Lot SD ng/mL (µg/L)	Between Lot CV (%)	Between Site SD ng/mL (µg/L)	Between Site CV (%)	Repro-ducibility SD ng/mL (µg/L)	Repro-ducibility CV (%)
Control 2	5.066	0.0799	1.6	0.1112	2.2	0.0000	0.0	0.0530	1.0	0.1131	2.2	0.1853	3.7
Control 3	22.325	0.3529	1.6	0.4566	2.0	0.0000	0.0	0.2632	1.2	0.4209	1.9	0.7613	3.4

[a] Standard deviation.
[b] Coefficient of variation.

Specimen Equivalency

Specimen equivalency was determined with the weighted Deming regression model using the Atellica IM Analyzer in accordance with CLSI Document EP35-ed2.[28]

Agreement of the specimen types may vary depending on the study design and population tested.

Tube (y) vs. Serum (x)	Regression Equation	Sample Interval	N[a]	r[b]
Plasma, dipotassium EDTA	y = 1.00x - 0.011 ng/mL (µg/L)	0.133–49.047 ng/mL (µg/L)	75	0.992
Plasma, lithium heparin	y = 1.01x - 0.007 ng/mL (µg/L)	0.133–49.047 ng/mL (µg/L)	75	0.996

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

Equimolarity

Equimolarity was assessed by testing various mixtures of complexed PSA (cPSA) and free PSA (fPSA) at set total PSA concentrations ranging from 0.800–20.000 ng/mL (µg/L) using the Atellica IM Analyzer. An equimolar assay should yield a consistent total PSA result with mixtures of fPSA and cPSA. Results demonstrated that the total concentration of PSA remained constant while varying the amounts of cPSA and fPSA at 11 different ratios. Linear regression slopes for the different total PSA concentrations (observed total PSA assay result versus varying ratios of fPSA:cPSA) were less than 0.10, which indicates equimolarity.

Interferences

Hemolysis, Icterus, Lipemia (HIL)

Interference testing was performed using the Atellica IM Analyzer in accordance with CLSI Document EP07-A2.[29] Interference as defined by % difference within + ~~bias greater than~~ 10% was not observed for the following substances when tested at analyte concentrations of 0.031–0.096 ng/mL (µg/L), 2.779–4.222 ng/mL (µg/L), and 6.935–10.246 ng/mL (µg/L).

Substance	Substance Test Concentration
Hemoglobin	1000 mg/dL (10.0 g/L)
Bilirubin, conjugated	60 mg/dL (711.6 µmol/L)
Bilirubin, unconjugated	60 mg/dL (711.6 µmol/L)
Lipemia (Intralipid)	3300 mg/dL (33.0 g/L)

Other Substances

Interference testing was performed using the Atellica IM Analyzer in accordance with CLSI Document EP07-A2.[29] Interference as defined by % difference within + ~~bias greater than~~ 10% was not observed for the following substances when tested at analyte concentrations of 0.036–0.121 ng/mL (µg/L) and 7.832–10.731 ng/mL (µg/L). Some substances were also tested at an analyte concentration of 3.154–4.115 ng/mL (µg/L).

Substance	Substance Test Concentration	Substance	Substance Test Concentration
Acetaminophen	15.6 mg/dL (1030 µmol/L)	Human Anti-Mouse Antibodies (HAMA)	2640 µg/L
Acetylsalicylic Acid	3.00 mg/dL (167 µmol/L)	Human IgG	2.5 g/dL
Alfuzosin hydrochloride	12 µg/mL (28.2 µmol/L)	Hydrochlorothiazide	0.113 mg/dL (3.8 µmol/L)
Alprazolam	0.0258 mg/dL (835 nmol/L)	Ibuprofen	21.9 mg/dL (1062 µmol/L)
Aminoglutethimide	72 µg/mL (310 µmol/L)	Ketoconazole	0.620 mg/dL (11.7 µmol/L)
Amlodipine Besylate	0.0075 mg/dL (0.132 nmol/L)	Leuprolide acetate	10 mg/dL (82.7 µmol/L)
Amoxicillin	5.40 mg/dL (148 µmol/L)	Lisinopril	0.0246 mg/dL (607 nmol/L)
Antinuclear antibodies (ANA)	≥ 1.0 AI	Megestrol acetate	250 µg/mL (650 µmol/L)
Atorvastatin	0.075 mg/dL (1.39 µmol/L)	Metformin hydrochloride	1.20 mg/dL (72.5 µmol/L)
Bicalutamide	60 µg/mL (139 µmol/L)	Methotrexate	300 mg/dL (6602 µmol/L)
Biotin	3500 ng/mL (14.3 µmol/L)	Mitomycin C	100 µg/mL (299 µmol/L)
Cholesterol	500 mg/dL (12.9 mmol/L)	Mitoxantrone	0.5 mg/mL (966 µmol/L)
Cimetidine	3.00 mg/dL (119 µmol/L)	Naproxen Sodium	36.0 mg/dL (1427 µmol/L)
Cisplatin dichloride	0.25 mg/mL (833 µmol/L)	Nitrofurantoin	0.213 mg/dL (8.94 µmol/L)
Ciprofloxacin	1.20 mg/dL (36.2 µmol/L)	Omeprazole	0.840 mg/dL (24.3 µmol/L)
Clomipramine hydrochloride	0.270 mg/dL (7.69 µmol/L)	Oxaliplatin	0.25 mg/mL (629 µmol/L)
Cyclophosphamide	800 µg/mL (2866 µmol/L)	Paclitaxel	4 ng/mL (4684 pmol/L)
Diethylstilbestrol	25 µg/mL (93.2 µmol/L)	Prazosin hydrochloride	85 ng/mL (202 nmol/L)

Substance	Substance Test Concentration	Substance	Substance Test Concentration
Docetaxel	5.5 µg/mL (6189 nmol/L)	Prednisone	1.65 µg/mL (4.6 µmol/L)
Doxazosin mesylate	4 µg/mL (7.3 µmol/L)	Total Protein	15.0 g/dL (150 g/L)
Doxycycline hyclate	1.80 mg/dL (35.1 µmol/L)	RF (Rheumatoid Factor)	1500 IU/mL
Doxorubicin hydrochloride	7 mg/dL (121 µmol/L)	Sildenafil citrate	0.2 mg/mL (300 µmol/L)
Dutasteride	0.3 µg/mL (568 nmol/L)	Silwet L-720 (Octamethylcyclotetrasiloxane)	30 mg/mL (101 mmol/L)
Estramustine phosphate	20 mg/dL (354 µmol/L)	Sulfamethoxazole	40.5 mg/dL (1600 µmol/L)
Fluoxetine hydrochloride	0.142 mg/dL (4.11 µmol/L)	Terazosin hydrochloride	1.45 mg/mL (3421 µmol/L)
Finasteride	25 µg/mL (67.1 µmol/L)	Trimethoprim	4.20 mg/dL (145 µmol/L)
Tamsulosin	1.0 µg/mL (2247 nmol/L)	Triptorelin	28 ng/mL (16.1 nmol/L)
5'-Fluorouracil	1.6 mg/mL (12.3 mmol/L)	Warfarin	7.50 mg/dL (243 µmol/L)
Flutamide	1.0 mg/dL (36.2 µmol/L)	Vinblastine sulfate	12 µg/mL (13.2 µmol/L)
Furosemide	1.59 mg/dL (48.1 µmol/L)	Vincristine sulfate	1.0 mg/mL (1083 µmol/L)
Goserelin acetate	7.2 µg/mL (5672 nmol/L)	Zoledronic Acid	667 ng/mL (2299 nmol/L)

Cross-Reactivity

Cross-reactivity was determined using the Atellica IM Analyzer in accordance with CLSI Document EP07-A2.[29] Cross-reactivity of samples spiked with various substances does not exceed 1% (or 10% bias, for CA 19-9) at an analyte concentration of approximately 0.038–0.105 ng/mL (µg/L), 3.058–4.090 ng/mL (µg/L), and 7.537–11.482 ng/mL (µg/L).

Substance	Substance Test Concentration
Alpha-fetoprotein (AFP)	10,000 ng/mL (8264 IU/mL)
Carcinoembryonic Antigen (CEA)	200 ng/mL (µg/L)
CA 19-9	1000 U/mL (kU/L)
Ferritin	10,000 ng/mL (22,470 pmol/L)
Human Chorionic Gonadotropin (HCG)	10,000 mIU/mL (10 IU/mL)
Human Kallikrein	100,000 ng/mL (100 µg/mL)
Prolactin	500 ng/mL (10,600 µIU/mL)
Prostatic Acid Phosphatase (PAP)	1000 ng/mL (µg/L)

Linearity

Linearity testing was performed using the Atellica IM Analyzer in accordance with CLSI Document EP06-ed2.[30]

The assay is linear for the analytical measuring interval of 0.009–50.000 ng/mL (µg/L).

High-Dose Hook Effect

High total PSA concentrations can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, no hook effect was observed up to 25,000 ng/mL (µg/L).

Standardization

The assay standardization is traceable to the World Health Organization (WHO) International Standard 17/100.

Assigned values for calibrators are traceable to this standardization.

Technical Assistance

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

siemens-healthineers.com

These instructions for use are intended to be used in countries where the CE mark is not required.

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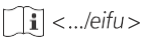
Definition of Symbols

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]

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	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]
UNITS C	Common Units	Proprietary	UNITS SI	International System of Units	Proprietary
YYYY-MM-DD	Date format (year-month-day)	N/A	**YYYY-MM**	Date format (year-month)	N/A
	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-*e*Note

[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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