SIEMENS

CE 0197

ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

Free PSA (fPSA)

Current revision and date [a]	Rev. 09, 2022-10		
Product Name	ADVIA Centaur® fPSA	REF	06862518
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system		
Materials Required but Not Provided	ADVIA Centaur fPSA Calibrator ADVIA Centaur Wash 1 (2 x 1500 mL) ADVIA Centaur Wash 1 (2 x 2500 mL)	REF REF REF	04846115 01137199 03773025
Specimen Types	Serum		
Assay Range	0.01–25.00 ng/mL (µg/L)		
Reagent Storage	2–8°C		
Reagent On-System Stability	60 days		

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

WARNING

The concentration of free 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 free PSA used. Values obtained with different assay methods cannot be used interchangeably. Use the ADVIA Centaur fPSA assay only with the ADVIA Centaur PSA assay to calculate the ratio of free PSA to total PSA (percent free PSA).

Intended Use

The ADVIA Centaur® free PSA (fPSA) assay is for *in vitro* quantitative measurement of free prostate-specific antigen in human serum using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems. The ADVIA Centaur fPSA assay is intended to be used in conjunction with the ADVIA Centaur PSA assay in men aged 50 years or older with total PSA values between 4 and 10 ng/mL and digital rectal exam (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. Prostate biopsy is required for the diagnosis of 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] The proteolytic activity of PSA is inhibited in the bloodstream by the formation of complexes with serine protease inhibitors.[4] The major immunoreactive forms of serum PSA include free PSA and complexes of PSA, primarily with α-1-antichymotrypsin (ACT), and small amounts of α-2-antitrypsin and inter-α-trypsin inhibitor.[5,6] The majority of free PSA in serum appears to be an inactive form that cannot complex with protease inhibitors, and may be a PSA-zymogen or a nicked form of PSA that is enzymatically inactive.[7–10] PSA also forms complexes with α-2-macroglobulin; however, this form is not immunoreactive because of encapsulation of PSA by the α-2-macroglobulin molecule.[6]

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.[11,12]

Immunometric assays have been designed to selectively measure free PSA, PSA complexed with ACT (cPSA), and total PSA (free PSA plus cPSA).[13–15] The proportion of free PSA in serum was found to be significantly higher in men with benign prostatic hyperplasia (BPH) than in men with prostate cancer.[16]

The percentage of free PSA determined by comparing the concentration of free PSA to the concentration of total PSA measured on the same instrument has been proposed as a way to improve the discrimination between BPH and prostate cancer in those men with levels of total PSA between 4–10 ng/mL.[14, 17,18]

Principles of the Procedure

The ADVIA Centaur fPSA assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses two monoclonal mouse antibodies. The first antibody, in the Lite Reagent, is an anti-PSA antibody labeled with acridinium ester. The second antibody, in the Solid Phase, is an anti-free PSA antibody labeled with biotin and bound to streptavidin paramagnetic particles.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur fPSA ReadyPack® primary reagent pack; Lite Reagent	5.8 mL/reagent pack monoclonal mouse anti-PSA antibody (~200 ng/mL) labeled with acridinium ester in buffered saline with preservatives	2–8°C	**Unopened**: Stable until the expiration date on carton **On-system**: 60 days
ADVIA Centaur fPSA ReadyPack primary reagent pack; Solid Phase Reagent	11.4 mL/reagent pack monoclonal mouse anti-fPSA antibody (~2.5 µg/mL) coupled to paramagnetic particles in buffered saline with preservatives	2–8°C	**Unopened**: Stable until the expiration date on carton **On-system**: 60 days
ADVIA Centaur fPSA calibrator[a]	2.0 mL/vial After reconstitution, low or high levels of fPSA in goat serum with sodium azide (< 0.1%) and preservatives	2–8°C	**Unopened**: Lyophilized–until the expiration date on the vial label **Reconstituted**: 21 days **On-system**: 8 hours

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur Wash 1[a] WASH 1	1500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 1 month
ADVIA Centaur Wash 1[a] WASH 1	2500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 1 month
ADVIA Centaur ReadyPack ancillary reagent pack; Multi-Diluent 2[b] M-DIL 2	10.0 mL/reagent pack goat serum with sodium azide (< 0.1%) and preservatives	2–8°C	**Unopened**: Until the expiration date on the pack **On-system**: 28 consecutive days after accessing the ancillary reagent pack

a See *Materials Required but Not Provided*

b See *Optional Materials*

Warnings and Precautions

Safety data sheets (MSDS/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.

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.

For Professional Use.

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

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

Mix all primary reagent packs by hand before loading them on the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, see the system operating instructions.

Note

- Discard the primary reagent packs at the end of the onboard stability interval.
- Do not use reagents beyond the expiration date.

Storing and Stability

Store the reagents upright at 2–8°C.

Protect reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light. Store unused reagent packs at 2–8°C away from heat and light sources.

All reagents are stable at 2–8°C until the expiration date on the packaging.

Specimen Collection and Handling

Serum is the recommended sample type for this assay.

The following recommendations for handling and storing blood samples are furnished by the Clinical and Laboratory Standards Institute (CLSI):[19]

- Collect all blood samples observing universal precautions for venipuncture.
- Allow samples to clot adequately before centrifugation.
- Keep tubes stoppered and upright at all times.
- Do not use samples 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.
- Freeze samples at or below -20°C if the sample is not assayed within 48 hours.
- Freeze samples only once and mix thoroughly after thawing.

The purpose of handling and storage information is to provide guidance to users. 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.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
06862518	1 ReadyPack primary reagent pack containing ADVIA Centaur fPSA Lite Reagent and Solid Phase ADVIA Centaur fPSA Master Curve cards	50

Materials Required but Not Provided

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

Item		Description	
REF	04846115	ADVIA Centaur fPSA Calibrator	2 vials of low calibrator CAL L 2 vials of high calibrator CAL H
REF	01137199 (112351)	ADVIA Centaur Wash 1 WASH 1	2 x 1500 mL/pack
REF	03773025	ADVIA Centaur Wash 1[a] WASH 1	2 x 2500 mL/pack

a for use with systems with 2500 mL capacity

Optional Materials

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

Item		Description	
REF	07948423 (110314)	ADVIA Centaur Multi-Diluent 2 M-DIL 2	2 ReadyPack ancillary reagent packs containing 10 mL/pack

Assay Procedure

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following actions:

- Dispenses 30 µL of sample into a cuvette.
- Dispenses 200 µL of Solid Phase and 100 µL of Lite Reagent and incubates for 9.25 minutes at 37°C.
- Separates, aspirates, and washes the cuvettes with Wash 1.
- Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.
- Reports results according to the selected option, as described in the system operating instructions.

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

Preparing the System

Ensure that the system has sufficient primary and ancillary reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Load the ReadyPack reagent packs in the primary reagent area using the arrows as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. For detailed information about loading reagents, refer to the system operating instructions.

If automatic dilution of a sample is required, load ADVIA Centaur Multi-Diluent 2 in the ancillary reagent entry.

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 detailed information about determining the minimum required volume, refer to the system operating instructions.

Note The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. For detailed information, refer to *Dilutions*.

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter. Remove particulates by centrifugation at 1000 x g for 15–20 minutes.
- Samples are free of bubbles.

On-System Stability

The ADVIA Centaur fPSA assay reagents are stable unopened until the expiration date on the carton or onboard the system for 60 days.

Performing Calibration

For calibration of the ADVIA Centaur fPSA assay, use the ADVIA Centaur fPSA calibrator. Perform the calibration as described in the calibrator instructions for use.

Calibration Frequency

Calibrate the assay at the end of the 28-day calibration interval.

Additionally, the ADVIA Centaur fPSA assay requires a two-point calibration:

- When changing lot numbers of primary reagent packs.
- When replacing system components.
- When quality control results are repeatedly out of range.

Performing Master Curve Calibration

The ADVIA Centaur fPSA assay requires a Master Curve calibration when using a new lot number of Lite Reagent and Solid Phase. For each new lot number of Lite Reagent and Solid Phase, use the barcode reader or keyboard to enter the Master Curve values on the system. The Master Curve card contains the Master Curve values. For detailed information about entering calibration values, refer to the system operating instructions.

Performing Quality Control

To monitor system performance and chart trends, as a minimum requirement, assay 2 levels of quality control material on each day that samples are analyzed. Assay quality control samples when performing a 2-point calibration. Treat all quality control samples the same as patient samples.

Siemens Healthcare Diagnostics recommends the use of commercially available quality control materials with at least 2 levels (low and high). For assistance in identifying a quality control material, refer to *ADVIA Centaur 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 Expected Values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.

Results

Calculation of Results

For detailed information about how the system calculates results, refer to the system operating instructions.

The system reports serum fPSA results in ng/mL (common units) or µg/L (SI units), depending on the units defined when setting up the assay. The conversion formula is 1 ng/mL = 1 µg/L.

Dilutions

The sample volume required to perform onboard dilution differs from the sample volume required to perform a single determination. Refer to the following information for the sample volume required to perform onboard dilutions:

Dilution	Sample Volume (µL)
1:2	75
1:5	30

The following information pertains to dilutions:

- Dilute and retest serum samples with fPSA levels greater than 25.0 ng/mL (µg/L) to obtain accurate results.
- The system can automatically dilute patient samples.
- For automatic dilutions, ensure that ADVIA Centaur Multi-Diluent 2 is loaded and set the system parameters as follows:

  Dilution point: ≤ 25.0 ng/mL (µg/L)

  Dilution factor: 2, 5

  For detailed information about automatic dilutions, refer to the system operating instructions.

Interpretation of Results

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

Limitations

Note

Do not interpret serum PSA or fPSA concentrations, regardless of the value, as definitive evidence for the presence or absence of prostate cancer. Prostate biopsy is required for the diagnosis of cancer. When changing PSA assays in the course of monitoring a patient, confirm baseline results using additional sequential testing.

Before treatment, patients with confirmed prostate carcinoma frequently have levels of fPSA within the range observed in healthy individuals. Elevated levels of fPSA can be observed in patients with nonmalignant diseases. Measurements of fPSA should always be used in conjunction with other diagnostic procedures, including information from the patient's clinical evaluation.

Specimens obtained from patients undergoing prostate manipulation, especially needle biopsy and transurethral resection, may show erroneously high results.[20] Care should be taken that fPSA 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.[21,22] 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.[23] Care should be taken when interpreting values from these individuals.

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.[24] PSA in serum and in seminal fluid exists primarily in complexed and free forms, respectively.[25] 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.

Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[13] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.

- Specimens that contain biotin at a concentration of 1500 ng/mL demonstrate a less than or equal to 10% change in results. Biotin concentrations greater than this may lead to incorrect results for patient samples.
- Results from patients taking biotin supplements or receiving high-dose biotin therapy should be interpreted with caution due to possible interference with this test.

Expected Values

A multicenter prospective clinical study was conducted to evaluate the effectiveness of the percent fPSA (fPSA/tPSA x 100) ratio as measured on the ADVIA Centaur system. The percent fPSA (% fPSA) result is used as an aid in distinguishing prostate cancer from benign prostate conditions in men 50 years or older with a total PSA of 4.0 to 10.0 ng/mL (µg/L) and with DRE findings not suspicious for cancer. The study consisted of 543 patients referred to an urologist for evaluation of prostate cancer from 27 clinical sites. All patients underwent a transrectal prostate biopsy. The diagnosis of prostate cancer or benign prostate disease for each patient was based on pathological examination of a minimum of six cores. Ethnic composition of the population studied included 436 (80.3%) Caucasian, 53 (9.8%) African-American, 40 (7.4%) Hispanic, 5 (0.9%) Asian, 1 (0.2%) Native American, and 8 (1.5%) from other ethnic groups. The table below displays the distribution of fPSA, tPSA and % fPSA by biopsy result.

fPSA, tPSA, and % fPSA Sample Statistics by Biopsy Result

	Biopsy Result	Count	Median	Interquartile Range	Mean	Standard Error of the Mean	Wilcoxon Rank Sum
fPSA (ng/mL)	Benign	343	1.10	0.64	1.18	0.031	< 0.0001
	Malignant	200	0.82	0.62	0.98	0.042	
tPSA (ng/mL)	Benign	343	5.84	1.90	6.17	0.077	< 0.3491
	Malignant	200	5.92	2.34	6.34	0.111	
% fPSA	Benign	343	17.59	9.15	19.37	0.456	< 0.0001
	Malignant	200	14.10	9.72	15.56	0.579	

Analysis of the mean values of percent fPSA for the benign and malignant disease groups indicates that a significant difference exists between the groups. The percent fPSA result may be used to provide an individual patient risk assessment of prostate cancer, or as a single cutoff to indicate the need for additional follow-up.

Individual Patient Risk Assessment

There is an increased probability of detecting prostate cancer upon biopsy as the PSA levels increase. In the PSA range of 4–10 ng/mL (µg/L), also known as the diagnostic gray zone, the percent fPSA (fPSA/tPSA x 100) is of increased utility. The lower the percentage of fPSA, the higher the risk of prostate cancer.

The probability of detecting prostate cancer upon biopsy by age and percent fPSA is shown below. The percentage of prostate cancer detected upon biopsy and by percent fPSA increased with the age.

Probability of Detecting Prostate Cancer on Biopsy by Age in Years

% fPSA	Age Groups (Years)			
	50–59	60–69	≥ 70	All Ages
≤ 10%	51.5% (33.5–69.2%)[a]	80.0% (63.1–91.6%)	85.7% (57.2–98.2%)	69.5% (58.4–79.2%)
11–18%	24.1% (15.1–35.0%)	31.3% (22.8–40.7%)	60.8% (46.1–74.2%)	35.1% (29.1–41.5%)
19–27%	10.3% (2.9–24.2%)	27.0% (16.6–39.7%)	38.6% (24.4–54.5%)	26.0% (19.1–33.9%)
> 27%	0.0% (0–28.3%)	25.9% (11.1–46.3%)	35.1% (20.2–52.5%)	27.4% (17.6–39.1%)

a (95% confidence interval)

Single Cutoff

A single cutoff may be used for men of all age groups. A cutoff of 27% results in the detection of 90% of prostate cancers (sensitivity) and avoids unnecessary biopsy in 15.5% of men without prostate cancer (specificity).

	Sensitivity		Specificity	
% fPSA Cutoff	**Percentage of Prostate Cancers Detected**	**95% CI[b]**	**Percentage of Biopsies Avoided in Men without Prostate Cancer[c]**	**95% CI**
23%	86.0% (172/200)[a]	80.4–90.5%	25.1% (86/343)[c]	20.6–30.0%
25%	88.0% (176/200)[a]	82.7–92.2%	19.5% (67/343)[c]	15.5–24.1%
27%	90.0% (180/200)[a]	85.0–93.8%	15.5% (53/343)[c]	11.8–19.7%
33%	95.5% (191/200)[a]	91.6–97.9%	7.6% (26/343)[c]	5.0–10.9%
51%	100% (200/200)[a]	98.5–100%	0.3% (1/343)[c]	0.0–1.6%

a Number of Prostate Cancers Detected / Total Number of Biopsy Positive

b 95% CI: 95% confidence interval

c Number of Biopsies Avoided, without Cancer / Total Number of Biopsy Negative

Each laboratory should establish its own expected values for percent free PSA based on its own patient population.

Note Do not interpret serum PSA or fPSA concentrations, regardless of the value, as definitive evidence for the presence or absence of prostate cancer. Prostate biopsy is required for the diagnosis of cancer. When changing PSA assays in the course of monitoring a patient, confirm baseline results using additional sequential testing.

Performance Characteristics

Analytical Measuring Range

The ADVIA Centaur fPSA assay measures free prostate-specific antigen concentrations from 0.01–25.00 ng/mL (µg/L).

Specificity

The potential interference of chemotherapeutic agents and therapeutic drugs was tested by adding these substances to serum pools containing fPSA ranging from 0.27 to 12.39 ng/mL (µg/L). All recoveries were within 10% of expected fPSA.

Substance	Amount Added (µg/mL)
Aminoglutethamide	72
Avodart	0.3
Bicalutamide	60
Cisplatin	100
Cyclophosphamide	700
Diethylstilbestrol	5
Doxorubicin	51.8
Estramustine Phosphate	200
Flomax	1
5-Fluorouracil	1000
Flutamide	10
Goserelin Acetate	7.2
Hytrin (Terazosin HCl)	10
Lupron (Leuprolide Acetate)	100
Megestrol Acetate	90
Methotrexate	30
Mitomycin C	100
Proscar	25
Uroxatrial	12
Vinblastine Sulfate	12

The fPSA assay cross-reactivity to complexed PSA was determined to be 0.23% at a concentration of 106.8 ng/mL PSA-ACT.

Interference testing was determined according to CLSI Document EP7-A2.[26]

Sensitivity

The ADVIA Centaur fPSA assay measures free PSA concentrations up to 25.00 ng/mL (µg/L). The sensitivity of the assay was estimated as the limit of detection (LoD) according to CLSI EP17-A.[27] Four serum pools containing very low levels of fPSA were assayed for ten days on two systems using two lots of reagents and calibrators. The ADVIA Centaur fPSA assay LoD is 0.01 ng/mL (µg/L). Functional sensitivity at 20% total CV was determined in a similar manner by assaying six serum pools for 10 days on 2 systems using 2 lots of reagents and calibrators. The ADVIA Centaur fPSA functional sensitivity is 0.01 ng/mL (µg/L).

Precision

Precision was evaluated according to CLSI protocol EP5-A2.[28] According to this protocol, the assay was run 2 times per day, for 20 days, using 2 reagent and calibrator lots on 2 ADVIA Centaur systems. The instruments were calibrated on the first run of day one. Assay results were calculated using a two-point calibration. The following results were obtained using 1 reagent lot and 1 system for five serum pools (n ≥ 160):

Mean (ng/mL) (µg/L)	Within run CV (%)	Between run CV (%)	Total CV(%)
0.42	3.2	1.6	4.3
0.96	2.0	1.7	3.7
2.33	2.6	1.2	3.5
13.71	2.8	0.8	4.0
19.44	5.3	5.2	7.9

Based on internal testing, the overall reproducibility is estimated to be ≤ 7% CV for samples tested (≤ 15.00 ng/mL) and includes multiple reagent lots, instruments, days, and replicates. Performance of the assay at individual laboratories may vary.

Interferences

Serum specimens that are...	Demonstrate ≤ 5% change in results up to...
hemolyzed	1000 mg/dL of hemoglobin
lipemic	1000 mg/dL of triglycerides
icteric	25 mg/dL of bilirubin (conjugated)
icteric	25 mg/dL of bilirubin (unconjugated)
biotin	1500 ng/mL of biotin

Dilution Recovery

Five serum samples in the range of 1.10 to 25.01 ng/mL (µg/L) of fPSA were diluted 1:2 and 1:5 with Multi-Diluent 2, and assayed for recovery and parallelism. The recoveries ranged from 90.9 to 114.7% with a mean of 102.4%.

Sample	Dilution	Observed ng/mL (µg/L)	Expected ng/mL (µg/L)	Recovery %
1	–	4.87		
	1:2	2.50	2.44	102.5
	1:5	1.02	0.97	105.2
	Mean			103.8
2	–	12.27		
	1:2	6.70	6.14	109.1
	1:5	2.81	2.45	114.7
	Mean			111.9
3	–	25.01		
	1:2	12.41	12.51	99.2
	1:5	4.79	5.00	95.8

Sample	Dilution	Observed ng/mL (µg/L)	Expected ng/mL (µg/L)	Recovery %
	Mean			97.5
4	–	3.47		
	1:2	1.81	1.74	104.0
	1:5	0.69	0.69	100.0
	Mean			102.0
5	–	1.10		
	1:2	0.53	0.55	96.4
	1:5	0.20	0.22	90.9
	Mean			93.6
Mean				**102.4**

High Dose Hook Effect

Patient samples with high free PSA levels can cause a paradoxical decrease in the RLUs (high-dose hook effect). In this assay, patient samples with free PSA levels as high as 10,000 ng/mL (µg/L) will assay greater than 25.0 ng/mL (µg/L).

Standardization

The ADVIA Centaur fPSA assay is traceable to World Health Organization (WHO) International Standard (96/668). A comparison over the range of the assay gave the following correlation:

ADVIA Centaur fPSA = 0.96 (WHO) + 0.11, r = 1.00

Troubleshooting

The following actions are recommended when you observe poor reproducibility of fPSA values at low levels or if you are not satisfied with assay performance:

- Ensure that the assay reagent and calibrator lot numbers and expiration dates match those entered in the system.
- Ensure that the calibrators, quality control materials, and assay reagents were prepared according to the recommended procedures.
- Ensure that the recommended sample collection and handling procedures were followed.
- Ensure that the recommended system cleaning procedures were followed.
- Ensure that Type II reagent water was used when operating the system.

  Note For information about reagent water, refer to the system operating instructions.
- Visually check the probe and tubing for obstructions, leaks, and deformities such as pinched or crimped tubing.
- Take further corrective action following established laboratory procedures.
- Calibrate the system using new assay reagents, calibrators, and quality control samples.
- Contact your local technical support provider or distributor for technical assistance.

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, please contact your local technical support provider or distributor.

siemens-healthineers.com

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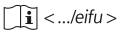
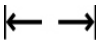
Trademarks

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
RxOnly	Prescription device (US only)	FDA[c]		Unique Device Identifier	5.7.10[b]
	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		Document face up[f]	1952[e]
YYYY-MM-DD	Date format (year-month-day)	N/A		International System of Units	Proprietary
	Target	Proprietary	**YYYY-MM**	Date format (year-month)	N/A
				Interval	Proprietary

Symbol	Symbol Title	Source	Symbol	Symbol Title	Source
	Handheld barcode scanner	Proprietary	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.	Proprietary
LOT DTL	Lot details	Proprietary	MC DEF	Master Curve definition	Proprietary
CAL LOT VAL	Calibrator lot value	Proprietary	CONTROL LOT VAL	Quality control 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 ISO 15223-1:2020-04

c Federal Register. Vol. 81, No 115. Wednesday, June 15, 2016. Rules and Regulations: 38911.

d IVDR REGULATION (EU) 2017/746

e International Standard Organization (ISO). ISO 7000 Graphical symbols for use on equipment.

f Indicates Assay-eNote

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