ARCHITECT Free PSA

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REF 7K71-20

en

Free PSA
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Read Highlighted Changes: Revised May 2019.

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

WARNING: The concentration of Free PSA in a given specimen, determined with 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 Free PSA assay used. Values obtained with different assay methods cannot be used interchangeably.

NAME

ARCHITECT Free PSA (Prostate Specific Antigen)

INTENDED USE

The ARCHITECT Free PSA assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of Free Prostate Specific Antigen (PSA) in human serum. The ARCHITECT Free PSA assay is intended to be used in conjunction with the ARCHITECT Total PSA assay in men aged 50 years or older with Total PSA values between 4 and 10 ng/mL and DRE non-suspicious for cancer to determine the % Free PSA value. The ARCHITECT % Free PSA value can be used as an aid in discriminating between prostate cancer and benign disease.

SUMMARY AND EXPLANATION OF THE TEST

Prostate specific antigen (PSA), a member of the human kallikrein gene family, is a serine protease with chymotrypsin-like activity.[1-3] The mature form of PSA is a single chain glycoprotein of 237 amino acids containing 7-8% carbohydrate as a single N-linked oligosaccharide side chain. PSA has a molecular weight of approximately 30,000 daltons.[1, 3, 4]

The major site of PSA production is the glandular epithelium of the prostate. PSA produced by the prostate is secreted into the seminal fluid in high concentrations. PSA is also present in urine and serum.[3] The function of PSA is the proteolytic cleavage of gel forming proteins in the seminal fluid resulting in liquefaction of the seminal gel and increased sperm mobility.[3, 5] Low levels of PSA are found in the blood as a result of leakage of PSA from the prostate gland. Increasing levels of PSA are associated with prostatic pathology; including prostatitis, benign prostatic hyperplasia (BPH), and cancer of the prostate.[6-9]

PSA occurs in three major forms in blood. The major immunodetectable form is PSA complexed with the serine protease inhibitor, alpha-1-antichymotrypsin (PSA-ACT). Uncomplexed, or Free PSA, is the other immunodetectable form of PSA in serum. The majority of Free PSA in serum appears to be an inactive form that cannot complex with protease inhibitors and may be either a PSA zymogen or an enzymatically-inactive, cleaved form of PSA. A third form of PSA, a complex with alpha-2-macroglobulin (AMG), is not detectable with current immunoassays for PSA due to the engulfment and subsequent masking of PSA epitopes by the alpha-2-macroglobulin molecule.[2, 3, 10]

Immunoassays have been designed to detect Free PSA, PSA-ACT complex, and Total PSA (immunodetectable forms: e.g., Free PSA and PSA-ACT).[10-12] Using these types of assays, the proportion of Free PSA in the serum was found to be significantly higher in patients with BPH than in patients with prostate cancer ($p < 0.00001$).[12] The proportion, or percent, of Free PSA determined by comparing the concentration of Free PSA to the concentration of Total PSA has been proposed as a way to improve the discrimination between BPH and prostate cancer, especially in those men with intermediate levels of total serum PSA.[10, 12-17]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Free PSA assay is a two step immunoassay to determine the presence of Free PSA in human serum, using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and anti-Free PSA coated paramagnetic microparticles are combined. The Free PSA present in the sample binds to the anti-Free PSA coated microparticles.
2. After washing, anti-PSA acridinium-labeled conjugate is added to create a reaction mixture.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of Free PSA in the sample and the RLUs detected by the ARCHITECT iSystem optics.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

REAGENTS

Kit Contents

ARCHITECT Free PSA 7K71

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT iSystems. Please contact your local distributor.

REF	7K71-25	7K71-20
Σ	100	400
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 mL

MICROPARTICLES Anti-Free PSA (mouse, monoclonal) coated Microparticles in TRIS buffer with protein (bovine) stabilizer. Preservative: antimicrobial agents.

CONJUGATE Anti-PSA (mouse, monoclonal) acridinium-labeled Conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: 10 ng/mL. Preservative: antimicrobial agents.

Other Reagents

PRE-TRIGGER SOLUTION ARCHITECT Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

WASH BUFFER ARCHITECT Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

NOTE: Bottle and volume varies based on order.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[18-21]

Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between kits.**
- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
  - To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
  - Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
  - Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.

For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Reagent Storage

When stored and handled as directed, reagents are stable until the expiration date.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened/ Opened*	2-8°C	Until expiration date	May be used immediately after removal from 2-8°C storage. Store in upright position.
On board	System temperature	30 days	Discard after 30 days. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

* Reagents may be stored on or off the ARCHITECT iSystem. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The ARCHITECT Free PSA assay file must be installed on the ARCHITECT iSystem from an ARCHITECT iSystem Assay CD-ROM prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.

For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.

For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

Alternate Result Units

Edit assay parameter "Result concentration units" to select an alternate unit.

Conversion formula:

(Concentration in Default result unit) x (Conversion factor) = (Concentration in Alternate result unit)

Default result unit	Conversion factor	Alternate result unit
ng/mL	1.0	µg/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

- Only human serum may be used in the ARCHITECT Free PSA assay.
- The instrument does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - grossly hemolyzed
  - obvious microbial contamination
- For accurate results, serum specimens should be free of fibrin, red blood cells, or other particulate matter. Centrifuge specimens containing fibrin, red blood cells, or particulate matter prior to use to ensure consistency in the results.
- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy may exhibit increased clotting time. If specimens are centrifuged before a complete clot forms, the presence of fibrin or particulate matter may cause erroneous results. Centrifuge specimens containing fibrin, red blood cells, or particulate matter. Note that interfering levels of fibrin may be present in samples that do not have obvious or visible particulate matter.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum collection tubes.
- It is recommended to obtain specimens for PSA testing prior to procedures involving manipulation of the prostate.
- Follow these package insert instructions as well as the specimen collection tube manufacturer's instructions for specimen collection and preparation for analysis. Refer to the specimen collection tube manufacturer's instructions for centrifugation time and speed.
- Insufficient processing of sample, or disruption of the sample during transportation may cause depressed results.

- If proper specimen collection and preparation cannot be verified, or if samples have been disrupted due to transportation or sample handling, an additional centrifugation step is recommended. Centrifugation conditions should be sufficient to remove particulate matter. Aliquots poured versus pipetted from specimen tube types that do not include serum separators are at higher risk of including particulates and generating depressed results.
- Failure to follow these instructions may result in depressed specimen results.
- Specimens must be mixed THOROUGHLY after thawing, by vortexing. Thawed samples containing red blood cells or particulate matter, **or which are hazy or cloudy in appearance** must be centrifuged prior to use to ensure consistency in the results.
- Inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum	2-8°C	≤ 24 hours

Serum should be separated from the clot within 3 hours from time of collection and stored at 2-8°C for up to 24 hours. The serum, if not tested within 24 hours, should be frozen at -20°C or colder.[22, 23] Avoid multiple freeze/thaw cycles.

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens that will not be assayed within 24 hours should be stored/shipped frozen. Prior to shipment, it is recommended that specimens be removed from the clot or serum separator.

PROCEDURE

Materials Provided

7K71 ARCHITECT Free PSA Reagent Kit

Materials Required but not Provided

- ARCHITECT Free PSA Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 7K71-01 ARCHITECT Free PSA Calibrators
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT Replacement Caps
- Pipettes or pipette tips (optional) to deliver the volumes specified on the patient or control order screen.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Materials Available but not Provided

- 7K71-10 ARCHITECT Free PSA Controls

Assay Procedure

- Before loading the reagent kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions about placing septums on bottles, refer to the **Reagent Handling** section of this package insert.
- Load the reagent kit on the ARCHITECT iSystem.
  - Verify that all necessary reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

  Maximum number of replicates sampled from the same sample cup: 10
  - Priority:

    Sample volume for first test: 140 µL

    Sample volume for each additional test from same sample cup: 90 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 90 µL
  - > 3 hours on board: Additional sample volume is required. Refer to the ARCHITECT System Operations Manual, Section 5 for information on sample evaporation and volumes.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT Free PSA Calibrators and Controls.
  - Mix calibrator(s) and controls by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 7 drops

    for each control: 7 drops
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

Specimens cannot be diluted for the ARCHITECT Free PSA assay. Specimens with a Free PSA value exceeding 30 ng/mL are flagged with the code “> 30.00”.

Calibration

- Test Calibrators 1 and 2 in duplicate. The calibrators should be priority loaded.

  A single replicate of each control level must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the respective control package insert.
- Calibration Range: 0 - 30 ng/mL

- Once an ARCHITECT Free PSA calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used or
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

Quality Control Procedures

The recommended control requirement for the ARCHITECT Free PSA assay is that a single sample of each control level be tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

The ARCHITECT Free PSA assay belongs to method group 6.

RESULTS

Calculation

The ARCHITECT Free PSA assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) to generate a calibration curve.

For information on alternate result units, refer to the **INSTRUMENT PROCEDURE, Alternate Result Units** section of this package insert.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

Calculation of ARCHITECT % Free PSA Value

- The ARCHITECT % Free PSA Value can be calculated when both ARCHITECT Free PSA and ARCHITECT Total PSA results are obtained for the same sample.
- The ARCHITECT iSystem (ARCHITECT software version 2.00 or higher) can automatically calculate a % Free PSA value. For information on configuring a calculated assay, refer to the ARCHITECT System Operations Manual, Section 2.
- The % Free PSA value is calculated by dividing the ARCHITECT Free PSA result by the ARCHITECT Total PSA result, then multiplying by 100.

LIMITATIONS OF THE PROCEDURE

- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits which employ mouse monoclonal antibodies.[24, 25] ARCHITECT Free PSA reagents contain a component that reduces the effect of HAMA reactive specimens. Additional clinical or diagnostic information may be required to determine patient status.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. 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.[26]
- The concentration of PSA in a given specimen, determined with assays from different manufacturers, can vary due to differences in assay methods, calibration, and reagent specificity.[3, 27, 28]
- Quality control samples may be produced by introducing seminal fluid PSA into a human serum matrix. PSA in serum and seminal fluid may exist in different forms. The concentration of PSA in these controls, determined with assays from different manufacturers, can vary due to differences in assay methods, calibration, reagent specificity, and the form of PSA that is present; therefore, it is important to use assay-specific values to evaluate control results.
- Digital rectal examination (DRE) may cause clinically significant changes in the Free PSA and Free/Total PSA ratio in some patients.[29] Additionally, prostatic massage, ultrasonography, cystoscopy, and needle biopsy may cause clinically significant elevations.[29, 30] Serum for Free PSA determinations should be drawn before performing prostatic manipulations. PSA levels may also be increased following ejaculation.[31]
- Active Free PSA in the serum at the time of blood sampling, can continue to complex with serum protease inhibitors, especially alpha-2-macroglobulin, resulting in a rapid decrease in PSA levels of the active form of Free PSA.[32]
- Hormonal therapy may affect PSA expression; therefore, a low PSA level after any treatment that includes hormonal therapy may not adequately reflect the presence of residual or recurrent disease.[33]
- The measurement of Free PSA or the Free/Total PSA ratio is not an absolute test for malignancy. The PSA values should be used in conjunction with information available from the clinical evaluation and other diagnostic procedures: e.g. symptoms, clinical impressions, digital rectal examination, transrectal ultrasound, etc. A prostatic biopsy is required for the diagnosis of cancer.

EXPECTED VALUES

[Values developed for the ARCHITECT i2000 analyzer.]

The distribution of ARCHITECT Free PSA values determined in apparently healthy males, males with BPH, and males with stage A and B prostate cancer is shown below.

Distribution of ARCHITECT Free PSA Values

		Percent (%)				
	Number of Subjects	0 - 0.5 (ng/mL)	>0.5 - 2.5 (ng/mL)	>2.5 - 5.0 (ng/mL)	>5.0 - 10 (ng/mL)	>10 (ng/mL)
Healthy Males	475	87.2	12.8	0.0	0.0	0.0
BPH	212	51.9	42.9	4.2	0.5	0.5
Stage A Prostate Cancer	26	38.5	42.3	11.5	3.8	3.8
Stage B Prostate Cancer	67	23.9	68.7	7.5	0.0	0.0

This distribution table is derived from 475 apparently healthy male subjects with no clinical evidence of prostate cancer, 212 males with BPH, and 93 males with active prostate cancer.

A prospective study of 430 subjects was conducted at nine clinical sites. A fixed cutoff of 26% was used to determine the sensitivity and specificity for subjects with a Total PSA range of 4 to 10 ng/mL and a DRE non-suspicious for cancer. The Total and Free PSA values were determined using the ARCHITECT Free PSA and ARCHITECT Total PSA assays. At the fixed cutoff of 26%, the ARCHITECT Free PSA assay yielded a sensitivity of 91.1% and a specificity of 18.2%.

The distribution of ARCHITECT % Free PSA values was determined for the same 430 subjects (307 biopsy negative and 123 biopsy positive). The % Free PSA values were divided into five groups by the following boundaries: ≤ 10, > 10-15, > 15-20, > 20-26, and > 26. The table below shows the % Free PSA values.

Distribution of ARCHITECT % Free PSA Values for Specimens with ARCHITECT Total PSA between 4 and 10 ng/mL

	Distribution of Subjects (%)					
	Number of Subjects	% Free PSA Ranges				
		≤ 10	>10-15	>15-20	>20-26	>26
Biopsy Negative	307	9.4	22.5	25.4	24.8	17.9
Biopsy Positive	123	27.6	30.9	17.9	15.4	8.1

The probabilities of prostate cancer given the value in specific ranges for % Free PSA were calculated based on a logistic regression model using the same group of subjects as above. Prostate cancer probabilities associated with % Free PSA values are dependent on the disease prevalence within the study population.[34]

In this study, the probabilities of prostate cancer are representative of a patient population for both screening and referral sites with an overall disease prevalence of approximately 29%.[35] The table below shows the distribution of cancer probabilities of % Free PSA using the same study population adjusted for different rates of disease prevalence.

Probability of Prostate Cancer by Disease Prevalence for Subjects with ARCHITECT Total PSA between 4 and 10 ng/mL and DRE Non-suspicious for Cancer

Disease Prevalence Rate (%)	% Free PSA Ranges				
	≤ 10	>10-15	>15-20	>20-26	>26
25[36]	44.0	32.9	23.4	16.0	10.6
29	48.6	37.1	26.9	18.6	12.5
35	56.0	44.2	33.1	23.5	16.1

The estimates of cancer probability may be influenced by the presence of other risk factors.

SPECIFIC PERFORMANCE CHARACTERISTICS

Assay results obtained in individual laboratories may vary from data presented.

Precision

[Values developed for the ARCHITECT i2000 analyzer.]

The ARCHITECT Free PSA assay precision is ≤ 8%. Precision was determined as described in the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-A.[37] Six samples, consisting of three serum based panels and three Free PSA controls, were assayed using three instruments, in replicates of two at two separate times per day for twenty days (n=80 for each sample), using a single lot of reagents and a single calibration. Data from this study are summarized in the following table.*

Reproducibility of ARCHITECT Free PSA

Sample	Instrument	Mean Free PSA (ng/mL)	Within Run		Total	
			SD	%CV	SD	%CV
Low Control	1	0.397	0.0076	1.9	0.0093	2.3
	2	0.400	0.0079	2.0	0.0085	2.1
	3	0.383	0.0080	2.1	0.0104	2.7
Medium Control	1	0.992	0.0130	1.3	0.0154	1.6
	2	1.000	0.0182	1.8	0.0209	2.1
	3	0.962	0.0248	2.6	0.0265	2.7
High Control	1	6.787	0.1175	1.7	0.1642	2.4
	2	6.966	0.1630	2.3	0.2094	3.0
	3	6.802	0.1241	1.8	0.1565	2.3
Panel 1	1	0.136	0.0029	2.1	0.0035	2.6
	2	0.139	0.0033	2.4	0.0035	2.5
	3	0.133	0.0030	2.3	0.0032	2.4
Panel 2	1	2.808	0.0447	1.6	0.0626	2.2
	2	2.887	0.0641	2.2	0.0788	2.7
	3	2.778	0.0591	2.1	0.0673	2.4
Panel 3	1	10.500	0.1853	1.8	0.3772	3.6
	2	10.952	0.3054	2.8	0.4507	4.1
	3	10.726	0.2662	2.5	0.4284	4.0

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Measurement Range

The measurement (reportable) range of the ARCHITECT Free PSA assay is 0.008 ng/mL to 30 ng/mL, as defined by the analytical sensitivity lower limit and the upper limit of the calibration range. For patient specimens with a Free PSA assay value exceeding 30 ng/mL refer to the **Specimen Dilution Procedures** section of this package insert.

Analytical Sensitivity

[Values developed for the ARCHITECT i2000 analyzer.]

The sensitivity of the ARCHITECT Free PSA assay was calculated to be less than 0.008 ng/mL. This sensitivity is defined as the concentration at two standard deviations above the mean RLU for the ARCHITECT Free PSA MasterCheck Level 0 and represents the lowest measurable concentration of Free PSA that can be distinguished from zero.

Analytical Specificity

[Values developed for the ARCHITECT i2000 analyzer.]

The specificity of the ARCHITECT Free PSA assay was determined by testing sera containing the following compounds. These compounds showed less than or equal to 10% interference in the ARCHITECT Free PSA assay at the levels indicated.

Interfering Substances

Test Compound	Concentration
Bilirubin	20 mg/dL
Hemoglobin	500 mg/dL
Total Protein	2.0 g/dL & 12.0 g/dL
Prostatic Acid Phosphatase	1000 ng/mL
Triglycerides	3000 mg/dL
Hytrin	20 µg/mL
Proscar	25 µg/mL
Flomax	1 µg/mL

Carryover

[Values developed for the ARCHITECT i2000 analyzer.]

No significant carryover (mean less than 4 PPM) was observed when a sample containing 7,167.5 ng/mL of Free PSA was assayed. To maintain optimum system performance and reduce the potential of carryover due to protein build up on the sample pipettor probe, it is important to follow the routine maintenance procedures defined in Section 9 of the ARCHITECT System Operations Manual, or, for troubleshooting information refer to the ARCHITECT System Operations Manual, Section 10.

High Dose Hook

[Values developed for the ARCHITECT i2000 analyzer.]

High dose hook is a phenomenon whereby very high level specimens may read within the dynamic range of the assay. For the ARCHITECT Free PSA assay, no high dose hook effect was observed when samples containing up to 2,400 ng/mL of Free PSA were assayed.

Accuracy by Correlation

The ARCHITECT Free PSA assay reagents were compared on the ARCHITECT i2000/i2000SR and the ARCHITECT i1000SR platforms. The results of specimen testing are shown below.

Statistical Method	Number of Observations	Intercept	Slope	Correlation Coefficient
Least Squares	149	0.00	0.99	1.000
Passing- Bablok*	149	0.00	0.98	1.000

* A linear regression method with no special assumptions regarding the distribution of the samples and the measurement errors.[38]

In this evaluation, serum specimens tested ranged from 0.009 ng/mL to 22.707 ng/mL, by the i1000SR platform.

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Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
CONJUGATE	Conjugate
CONTROL NO.	Control Number
GTIN	Global Trade Item Number
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCT OF IRELAND	Product of Ireland
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
TRIGGER SOLUTION	Trigger Solution
WASH BUFFER	Wash Buffer


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