ARCHITECT Total PSA

REF 7K70-25
REF 7K70-20
REF 7K70-35
REF 7K70-30

en

Total PSA
7K70
G47685R07
B7K700

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 Total 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 Total PSA assay used. Values obtained with different assay methods, including Abbott PSA assays, cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining Total PSA levels serially is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

NAME

ARCHITECT Total PSA (Prostate Specific Antigen)

INTENDED USE

The ARCHITECT Total PSA assay is a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of Total PSA (both Free PSA and PSA complexed to alpha-1-antichymotrypsin) in human serum:

1. As an aid in the detection of prostate cancer when used in conjunction with digital rectal exam (DRE) in men 50 years or older. Prostatic biopsy is required for diagnosis of cancer.
2. As an adjunctive test to aid in the management of prostate cancer patients.

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. 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, 8, 37, 38]

The major site of PSA production is the glandular epithelium of the prostate. PSA has also been found in breast cancers, salivary gland neoplasms, periurethral and anal glands, cells of the male urethra, breast milk, blood and urine.[1, 2] PSA produced in the prostate is secreted into the seminal fluid in high concentrations. A major function of PSA is the proteolytic cleavage of gel-forming proteins in the seminal fluid, resulting in the liquefaction of the seminal gel and increased sperm mobility.[1] Low levels of PSA are found in the blood as a result of leakage of PSA from the prostate gland. Increasing levels of serum PSA are associated with prostatic pathology, including prostatitis, benign prostatic hyperplasia (BPH), and cancer of the prostate.[1, 3-7]

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. Equimolar-response PSA assays have an equivalent response to both Free PSA and PSA-ACT.[1] The ARCHITECT Total PSA assay is an equimolar assay. A third form of PSA, a complex with alpha-2-macroglobulin, is not detectable with current immunoassays for PSA due to the engulfment and subsequent masking of PSA epitopes by the alpha-2-macroglobulin molecule.[1, 8, 9]

Prostate cancer is the most frequently diagnosed cancer and the second leading cause of cancer deaths in men in the United States.[10] Early diagnosis of carcinoma of the prostate is hindered by the lack of symptoms in men with localized tumors. Therefore, early detection requires a simple, safe, and inexpensive test for the disease in asymptomatic men. The traditional method for detection of prostate cancer is the digital rectal examination (DRE). However, only 30 to 40% of cancers detected by DRE screening are expected to be confined to the prostate. The frequent finding of locally advanced prostate cancer in screened patients may be due to the inability of DRE to detect tumors of small volume that are most likely to be confined to the prostate.[11] Since patients with small tumors are believed to have the best prognosis, it can be concluded that DRE has limited sensitivity in detecting those tumors with the greatest potential for cure.[12]

In a 1990 publication by Cooner et al., data was presented regarding the clinical use of other diagnostic modalities such as prostate ultrasonography and serum prostate specific antigen for early detection of prostate cancer. This study found that there was a significant increase in predictability for cancer when the DRE and PSA tests were abnormal.[13] Several other studies have shown that the measurement of serum PSA concentrations offers several advantages in the early detection of prostate cancer. The procedure is more acceptable to patients, the result is objective and quantitative, and is independent of the examiners skill. In several recent studies of healthy men 50 years or older, serum PSA levels had the greatest ability to predict prostate cancer. These studies concluded that not only is serum PSA measurement a useful addition to rectal examination and ultrasonography in the detection of prostate cancer, but that it is also the most accurate of the three tests for this purpose.[14, 15] In January 1992, the American Urological Association endorsed annual examination with DRE and PSA, for early detection of prostate cancer, beginning at age 50.[16] This was reaffirmed by the American Cancer Society in November 1992.[17] The combined use of DRE and PSA has been shown to result in an increased detection of early stage prostate cancer; however, the benefit of early detection on patient outcome has not been proven and is the subject of ongoing clinical trials.[4-7, 13-15, 18, 19]

PSA testing can have significant value in detecting metastatic or persistent disease in patients following surgical or medical treatment of prostate cancer. Persistent elevation of PSA following treatment, or an increase in a post-treatment PSA level is indicative of recurrent or residual disease. PSA testing is widely accepted as an adjunctive test in the management of prostate cancer patients.[3-7]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Total PSA assay is a two-step immunoassay to determine the presence of Total PSA (both Free PSA and PSA complexed to alpha-1-antichymotrypsin) in human serum using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample and anti-PSA coated paramagnetic microparticles are combined to create a reaction mixture. The PSA present in the sample binds to the anti-PSA coated microparticles.
2. After washing, anti-PSA acridinium-labeled conjugate is added. Pre-Trigger and Trigger Solutions are then added to the reaction mixture.
3. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of Total 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 Total PSA 7K70

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

REF	7K70-25	7K70-20	7K70-35	7K70-30
Σ	100	400	500	2000
MICROPARTICLES	1 x 6.6 mL	4 x 6.6 mL	1 x 27.0 mL	4 x 27.0 mL
CONJUGATE	1 x 5.9 mL	4 x 5.9 mL	1 x 26.3 mL	4 x 26.3 mL

MICROPARTICLES Anti-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

MULTI-ASSAY MANUAL DILUENT 1 x 100 mL ARCHITECT Multi-Assay Manual Diluent, REF 7D82-50, containing phosphate buffered saline solution. Preservative: antimicrobial agent.

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.[20-23]

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 Total 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 Total 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.
- 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.
- 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.
- 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

If testing will be delayed more than 24 hours, specimens should be removed from the clot or serum separator and stored frozen at -20°C or colder.[24, 25]

NOTE: Samples which may be tested for Free PSA should be removed from the clot within 3 hours.

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

7K70 ARCHITECT Total PSA Reagent Kit

Materials Required but not Provided

- ARCHITECT Total PSA Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 7K70-01 ARCHITECT Total PSA Calibrators
- 7D82-50 ARCHITECT Multi-Assay Manual Diluent
- 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

- 7K70-10 ARCHITECT Total 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: 100 µL

    Sample volume for each additional test from same sample cup: 50 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 150 µL

    Sample volume for each additional test from same sample cup: 50 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 Total 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: 4 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 with a Total PSA value exceeding 100 ng/mL are flagged with the code "> 100.000" and may be diluted using either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

The system performs a 1:10 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.

Dilutions other than 1:10 should be done manually.

Manual Dilution Procedure

Suggested dilution: 1:20

1. Add 50 µL of the patient specimen to 950 µL of ARCHITECT Multi-Assay Manual Diluent.
2. The operator must enter the dilution factor in the Patient or Control order screen. All assays selected for that order will be diluted. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The dilution should be performed so that the diluted result reads greater than 0.4 ng/mL.

For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

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 - 50 ng/mL.
- The assay protocol allows for the range to be extended to 100 ng/mL.
- Once an ARCHITECT Total 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 Total PSA assay is that a single replicate 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 Total PSA assay belongs to method group 1.

RESULTS

Calculation

The ARCHITECT Total 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.

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 such as ARCHITECT Total PSA that employ mouse monoclonal antibodies.[26, 27] ARCHITECT Total 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.[28]
- 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.[1, 29, 30]

- 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.
- 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.[31]
- In most instances, specimens obtained from patients immediately following digital rectal examination show no clinically significant increases in PSA levels.[32] However, prostatic massage, ultrasonography, and needle biopsy may cause clinically significant elevations.[33] PSA levels may also be increased following ejaculation.[34]
- 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.[35]
- Serum PSA concentrations should not be interpreted as absolute evidence for the presence or absence of prostate cancer. Elevated concentrations of PSA may be observed in the serum of patients with benign prostatic hyperplasia or other nonmalignant disorders as well as in prostate cancer. Furthermore, low PSA concentrations are not always indicative of the absence of cancer. The PSA value should be used in conjunction with information available from clinical evaluation and other diagnostic procedures such as DRE. Some early cases of prostate cancer will not be detected by PSA testing; the same is true for DRE. Prostatic biopsy is required for the diagnosis of cancer.

EXPECTED VALUES FOR DETECTION OF PROSTATE CANCER

[Values developed for the ARCHITECT i2000 analyzer.]

A prospective study was conducted at seven clinical sites to demonstrate the usefulness of PSA in the detection of prostate cancer when used in conjunction with DRE. All clinical data presented supporting the detection claim were generated using the ARCHITECT iSystem and ARCHITECT Total PSA assay reagents. A total of 531 men 50 years of age or older participated in the study. All subjects were biopsied based on an initial elevated PSA value and/or suspicious DRE result. A distribution of the ARCHITECT Total PSA results is presented in the following table:

Distribution of Results from ARCHITECT Total PSA

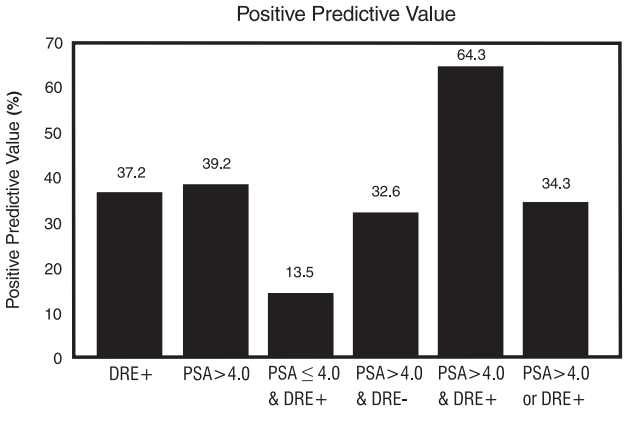
	PSA ≤ 4.0	PSA > 4.0	Total
DRE-[b]	32	319	351
	6.0%	60.1%	66.1%
DRE+[a]	96	84	180
	18.1%	15.8%	33.9%
Total	128	403	531
	24.1%	75.9%	100.0%

NOTE: 499 patients tested positive by DRE and/or PSA.

[a] DRE+: Digital Rectal Examination (Suspicious for cancer)

[b] DRE-: Digital Rectal Examination (Not suspicious for cancer)

The positive predictive values for various combinations of DRE and PSA are presented graphically in the figure below and table below.



Positive Predictive Values

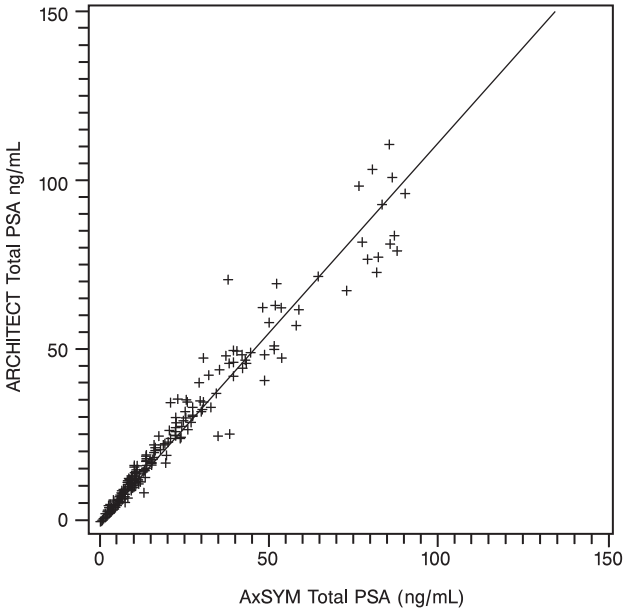
Detection Method	Positive Predictive Value (%)*	Number of Subjects with Cancer/Number of Subjects Suspicious for Cancer
DRE+	37.2 (30.1-44.7)	67/180
PSA > 4.0	39.2 (34.4-44.2)	158/403
PSA ≤ 4.0 and DRE+	13.5 (7.4-22.0)	13/96
PSA > 4.0 and DRE-	32.6 (27.5-38.0)	104/319
PSA > 4.0 and DRE+	64.3 (53.1-74.4)	54/84
PSA > 4.0 or DRE+	34.3 (30.1-38.6)	171/499

* 95% Confidence Interval (Lower Limit - Upper Limit)

Cancers were detected in 177 of the 531 subjects. The overall cancer detection rate was 96.6% (171/177) when at least one test was suspicious, 30.5% (54/177) when both tests were suspicious, 58.8% (104/177) for PSA alone, and 7.3% (13/177) for DRE alone.

CORRELATION

To demonstrate that the ARCHITECT Total PSA assay results are comparable to the results from the AxSYM Total PSA assay, a least squares linear regression analysis was performed comparing the PSA values from both assays for 1,798 clinical specimens. The analysis yielded a correlation coefficient of 0.987, a slope of 1.06, and a Y-intercept of 0.344 for the specimens covering the range up to 100 ng/mL, as shown in the following figure:



These results demonstrate that the ARCHITECT Total PSA assay yields equivalent results compared to those obtained using the AxSYM Total PSA assay.

Serum PSA concentrations, regardless of the value, should not be interpreted as definitive evidence for the presence or absence of prostate cancer. In addition, PSA testing should be done in conjunction with DRE because PSA and DRE together detected the greatest number of cancers. Prostatic biopsy is required for the diagnosis of cancer.

EXPECTED VALUES

[Values developed for the ARCHITECT i2000 analyzer.]

The distribution of ARCHITECT Total PSA values determined in 2,287 specimens is shown in the following table.

Distribution of ARCHITECT Total PSA Values

			Percent (%)				
		Number of Subjects	0 - 4.0 (ng/mL)	> 4.0 - 10 (ng/mL)	>10 - 30 (ng/mL)	>30-60 (ng/mL)	> 60 (ng/mL)
Apparently Healthy Subjects	Females	296	100.0	0.0	0.0	0.0	0.0
	Males Ages 40 to 49	99	100.0	0.0	0.0	0.0	0.0
	Males Ages 50 to 59	120	97.5	2.5	0.0	0.0	0.0
	Males Ages 60 to 69	123	93.5	6.5	0.0	0.0	0.0
	Males Ages 70 to 79	124	91.9	7.3	0.8	0.0	0.0
Nonmalignant Disease	BPH	352	42.6	42.3	12.8	1.1	1.1
	Cirrhosis	89	94.4	3.4	1.1	0.0	1.1
	Genitourinary	151	90.7	7.3	1.3	0.7	0.0
	Prostatitis	142	46.5	40.1	11.3	1.4	0.7
	Renal	140	90.0	5.7	2.9	1.4	0.0
Malignant Disease	Prostate Stage A	94	46.8	30.9	17.0	1.1	4.3
	Prostate Stage B	166	30.1	44.0	23.5	0.6	1.8
	Prostate Stage C	141	26.2	22.7	29.1	12.8	9.2
	Prostate Stage D	95	15.8	12.6	32.6	10.5	28.4
	Genitourinary	155	92.9	3.9	1.9	0.6	0.6

In this study, 95.5% of the specimens from apparently healthy male subjects (n=466) had values of 4.0 ng/mL or less.

It is recommended that each laboratory establish its own expected reference range for the population of interest.

The malignant disease portion of the distribution table is derived primarily from carcinoma patients representing both active (clinical evidence of disease progression) and inactive (no clinical evidence of disease progression) disease states. When changing PSA assay methods in the course of monitoring a patient, additional sequential testing should be carried out to confirm baseline values.

SPECIFIC PERFORMANCE CHARACTERISTICS

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

Precision

[Values developed for the ARCHITECT i2000 analyzer.]

ARCHITECT Total PSA assay precision is ≤ 8%. Precision was determined as described in the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-A.[36] Six samples, consisting of three serum based panels and three Total 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 Total PSA

		Mean Total	Within Run		Total	
Sample	Instrument	PSA (ng/mL)	SD	%CV	SD	%CV
Low Control	1	0.498	0.0087	1.8	0.0109	2.2
	2	0.511	0.0203	4.0	0.0237	4.6
	3	0.504	0.0131	2.6	0.0194	3.9
Medium Control	1	4.030	0.1036	2.6	0.1107	2.7
	2	4.104	0.1517	3.7	0.1836	4.5
	3	4.101	0.1218	3.0	0.1714	4.2
High Control	1	24.565	0.7187	2.9	0.8121	3.3
	2	24.558	1.0663	4.3	1.1691	4.8
	3	24.210	0.7742	3.2	1.5808	6.5
Panel 1	1	4.130	0.1129	2.7	0.3230	7.8
	2	4.109	0.1479	3.6	0.1665	4.1
	3	4.139	0.1042	2.5	0.2099	5.1
Panel 2	1	49.191	1.6925	3.4	1.8405	3.7
	2	46.943	2.0034	4.3	2.6271	5.6
	3	47.770	1.5792	3.3	3.4934	7.3
Panel 3	1	66.952	2.0804	3.1	4.1157	6.1
	2	62.631	3.1461	5.0	3.2269	5.2
	3	61.632	1.5634	2.5	5.5307	9.0

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

Measurement Range

The measurement (reportable) range of the ARCHITECT Total PSA assay is 0.008 ng/mL to 100 ng/mL, as defined by the analytical sensitivity lower limit and the upper limit of the extended calibration range. For patient specimens with a Total PSA assay value exceeding 100 ng/mL refer to the **Specimen Dilution Procedures** section of this package insert.

Recovery

[Values developed for the ARCHITECT i2000 analyzer.]

Known concentrations of serum PSA were added to ten normal human serum samples. Each sample was spiked at a low and a high level. The concentration of Total PSA was determined using the ARCHITECT Total PSA assay and the resulting percent recovery was calculated. The mean recovery was 95.9% with values ranging from 89.8% to 99.6%.

Sensitivity

[Values developed for the ARCHITECT i2000 analyzer.]

Functional

Functional sensitivity is defined as the lowest concentration that can be measured with an inter-assay coefficient of variation (CV) less than or equal to 20%. The calculated %CV for one reagent lot from all sites was plotted against the mean concentration of each panel. A parametric curve was fitted through the data, and the functional sensitivity was determined to be less than 0.05 ng/mL, which corresponded to less than 20% CV on the fitted curve.

Analytical

The analytical sensitivity of the ARCHITECT Total 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 Total PSA MasterCheck Level 0 and represents the lowest measurable concentration of Total PSA that can be distinguished from zero.

Analytical Specificity

[Values developed for the ARCHITECT i2000 analyzer.]

The analytical specificity of the ARCHITECT Total PSA assay was determined by testing sera containing the following compounds. These compounds showed less than or equal to 10% interference in the ARCHITECT Total 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	10 µg/mL
Proscar	25 µg/mL
Flomax	1 µg/mL

CHEMOTHERAPEUTIC AGENTS

Test Compound	Concentration
Cyclophosphamide	700 µg/mL
Diethylstilbestrol	2 µg/mL
Doxorubicin-HCl	16 µg/mL
Estramustine Phosphate	200 µg/mL
Flutamide	10 µg/mL
Goserelin Acetate	100 ng/mL
Lupron	100 µg/mL
Megestrol Acetate	90 µg/mL
Methotrexate	30 µg/mL

Carryover

[Values developed for the ARCHITECT i2000 analyzer.]

No detectable carryover (less than 0.5 PPM) was observed when a sample containing 16,791 ng/mL of PSA was assayed.

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 Total PSA assay, no high dose hook effect was observed when samples containing up to approximately 48,000 ng/mL of PSA were assayed.

Accuracy by Correlation

The ARCHITECT Total 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	151	-0.06	1.05	0.996
Passing-Bablok*	151	-0.03	1.04	0.996

* A linear regression method with no special assumptions regarding the distribution of the samples and the measurement errors.[39]

In this evaluation, serum specimens tested ranged from 0.046 ng/mL to 81.710 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
MULTI-ASSAY MANUAL DILUENT	Multi-Assay Manual Diluent
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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