Brown Clinic Northridge
511 14th Ave. NE
Watertown, SD

Brown Clinic
506 First Ave. SE
Watertown, SD

BROWN CLINIC
LABORATORY PROCEDURE MANUAL

PROCEDURE: Total Prostate Specific Antigen

CAUTION: United States Federal law restricts this device to sale and distribution by or on the order of a physician, or to a clinical laboratory; and use is restricted to, by or on the order of a physician.

Warning: The concentration of 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 PSA assay used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining 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.

PURPOSE:

The PSA method for the Dimension Integrated chemistry system with the heterogeneous immunoassay module is an *in vitro* diagnostic test intended to quantitatively measure prostate specific antigen (PSA) in **human serum and plasma**:

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. Prostate biopsy is required for diagnosis of cancer.
2. As an aid in the management (monitoring) of prostate cancer patients.

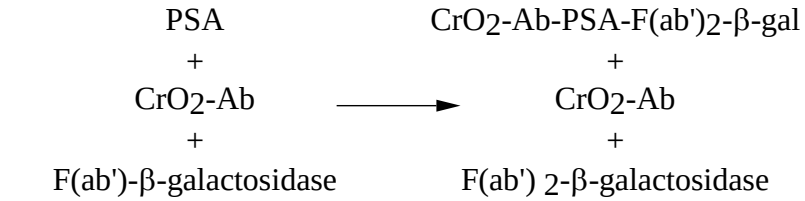
PRINCIPLE:

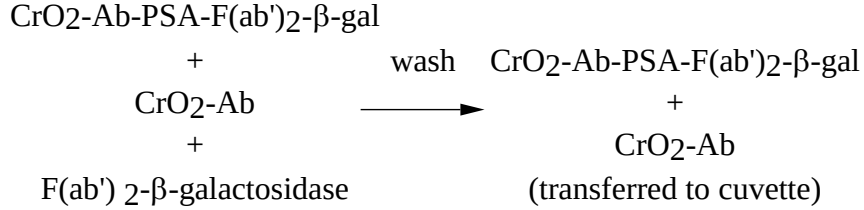
Prostate specific antigen (PSA) is a serine protease of approximately 30,000 Daltons produced by the epithelial cells of the prostate gland.[1,2] The level of PSA in serum and other tissues is normally very low. In malignant prostate disease (prostatic adenocarcinoma) and in non-malignant disorders such as benign prostate hypertrophy (BPH) and prostatitis, the serum level of PSA may become elevated.[3]

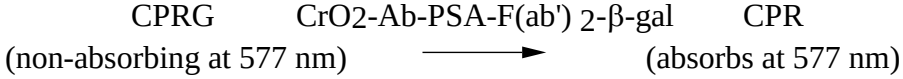
In Serum, PSA exists primarily as three forms: complexed with either a1-antichymotrypsin (ACT) or α2-macroglobulin and free.[4,5] The PSA protein associated with α2-macroglobulin is encapsulated and unavailable for measurement by current immunoassay systems. The Dimension® PSA assay measures both the free and the ACT bound components of serum PSA. The specificity of PSA to prostate tissue makes it a significant marker in the early detection and management of prostate diseases.

Prostate cancer is the most common type of cancer found in men in the United States and the second leading cause of male cancer mortality, accounting for more than 30,000 deaths in 1999.[6] Prior to the use of PSA for early detection of prostate cancer, the traditional method of digital rectal examination (DRE) detected considerably fewer tumors.[3,7] The most sensitive method for early detection of prostate cancer uses both DRE and PSA. The American Cancer Society and The American Urological Association (AUA) recommend that early detection of prostate cancer should be offered to asymptomatic men 50 years of age an older with an estimated life expectancy of more than 10 years. An abnormal DRE and/or an elevated PSA may suggest the presence of prostate cancer, however a prostate biopsy is required for final diagnosis.
PSA testing is also accepted as a test in the monitoring of previously diagnosed prostate cancer patients.[9,10] Serum levels of PSA are most useful when sequential values are obtained and monitored over time. After complete removal of the prostate gland (radical prostatectomy), PSA levels should decline to a very low or nondetectable level. A rise of the serum PSA level in prostatectomy patients indicates residual prostate tissue, recurrence or metastasis of the disease.[11] Serum PSA levels during radiation treatment should decline and remain at baseline while the patient is in remission.[12]

The PSA method is a one step enzyme immunoassay based on the "sandwich" principle. Sample is incubated with chromium dioxide particles coated with monoclonal antibodies specific for a binding site on PSA, and conjugate reagent (β-galactosidase labelled monoclonal antibodies specific for a second binding site on the PSA molecule) to form a particle/PSA/conjugate sandwich. Unbound conjugate and analyte are removed by magnetic separation and washing. The sandwich bound β-galactosidase is combined with the chromogenic substrate chlorophenol red-β-d galactopyranoside (CPRG). Hydrolysis of CPRG releases a chromophore (CPR). The color change measured at 577 nm due to formation of CPR is directly proportional to the concentration of PSA present in the patient sample.







INSTRUMENT, REAGENTS & SUPPLIES:

Wells[a]	Form	Ingredient	Concentration[b]	Source

1	Liquid	PSA Ab-β-galactosidase[c]	0.09 mg/mL	Mouse, monoclonal
2	Liquid	Chrome diluent	4.8 mg/ml	
3	Tablet[d]	Antibody-CrO_2[c]	1.8 mg/mL	Mouse, monoclonal
4,5,6	Tablet[d]	CPRG	10.3 mg/mL	
7	Liquid	Substrate diluent	42 mg/mL	

a. Wells are numbered consecutively from the wide end of the cartridge.

b. Nominal value in hydrated cartridge.

c. Antibody titer and conjugate activity may vary from lot to lot.

d. Tablets contain excipients, buffers, and stabilizers.

Risk and Safety:

H317

9280, P272, P302+P352, P333, P501

Warning!

May cause an allergic skin reaction.

Wear protective gloves/protective clothing/eye protection/face protection. Contaminated work clothing should not be allowed out of the workplace. IF ON SKIN: Wash with plenty of soap and water. IF skin irritation or rash occurs: Get medical advice/attention. Dispose of contents and container in accordance with all local, regional, and national regulations.

Contains: 5-chloro-2-methyl-3(2h)-isothiazolone mixture with 2-methyl-3(2h)-isothiazolone.

Safety data sheets(MSDS/SDS) available on www.siemens.com/healthcare

Precautions:

Irritant. Contains mixture of 5-chloro-2-methyl-cH-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one (3:1)

Used cuvettes contain human body fluids; handle with appropriate care to avoid skin contact or ingestion.

Contains Sodium Azide (<0.1%) as a preservative. Sodium azide can react with copper or lead pipes in drain lines to form explosive compounds. Dispose of properly in accordance with local regulations.

For *in vitro* diagnostic use

Safety Data Sheets (SDS/MSDS) can be found at www.siemens.com/healthcare

Reagent Preparation: Mixing and diluting are automatically performed by the Dimension® system.

REAGENT STORAGE & STABILITY:

Store at 2-8°C.

Expiration: Refer to carton for expiration date of individual unopened reagent cartridges. Sealed or unhydrated cartridge wells on the instrument are stable for 30 days. Once wells 1, 3 and 7 have been entered by the instrument, they are stable for 15 days. Once wells 4, 5 and 6 have been entered by the instrument, they are stable for 5 days.

SPECIMEN REQUIREMENTS:

Serum and heparinized plasma can be collected by normal procedures.[13] Follow the instruction provided with your specimen collection device for use and processing.

Specimens should be free of particulate matter. To prevent the appearance of fibrin in serum samples, complete clot formation should take place before centrifugation. Clotting time may be increased due to thrombolytic or anticoagulant therapy.

Specimens should be separated from cells within 3-4 hours.

An erroneously elevated PSA level can be observed if the serum specimen from a patient is collected following digital rectal examination (DRE), needle biopsy or transurethal resection.[14]

Each laboratory should determine the acceptability of its own blood collection tubes and serum separation products. Variations in these products may exist between manufacturers and, at times, from lot to lot.

Specimen:

patient preparation: no preparation required
specimen type: serum or heparinized plasma
stability: Specimens may be refrigerated at 2-8°C for up 8 hours.
For longer storage, samples may be frozen at -20°C.[15]
For extended storage samples are stable for at least 4 moths at -80°C. Mix thoroughly after thawing. Avoid repeated freezing and thawing.

CONTROLS:

At least once daily run solutions at two levels of a quality control material with known concentrations.

For further details, refer to your Dimension® system manual. The result obtained should fall within limits defined by the day-to-day variability of the system as measured in the user's laboratory. If the results fall outside the laboratory's acceptable limits, follow the procedure in the quality control policy.

PROCEDURE:

Materials Needed

PSA Flex® reagent cartridge, Cat. No. RF451

Reaction Vessels, Cat. No. RXV1A

Chemistry Wash, Cat. No. RD701

Sample Probe Cleaner, Cat. No. RD703

T/F PSA Calibrator Cat. No. RC452

Quality control procedures

Test Steps

Sampling, reagent delivery, mixing, separation, processing and printing of results are automatically performed by the Dimension® system with the heterogeneous immunoassay module. For details of this processing, refer to your Dimension® system manual.

Test Conditions

Reaction Vessel

• Sample size	40 µL
• Antibody- CrO_2	30 µL
• Antibody-β-galactosidase	50 µL
• Temperature	37.0° C
• Incubation period	9 minutes

Reaction Cuvette

• Transfer Volume	60 µL
• CPRG Reagent Volume	150 µL
• Temperature	37.0 ± 0.1°C
• Reaction period	5 minutes
• Wavelength	577 and 700 nm
• Type of measurement	Bichromatic Rate
• Units	ng/mL[µg/L]

Backup Process:
Refer to Brown Clinic Back-up Policy

Calibration

The general calibration procedure is described in your Dimension® system manual (also see Appendix B).

The following information should be considered when calibrating the PSA method:

Assay Range	0.13 - 100.0 ng/mL [µg/L)
Reference Material	PSA Calibrator Cat. No. RC452
Suggested Calibration Levels	0.0, 4.0, 10.0, 45.0, 105.0 ng/mL[µg/L]
Calibration Scheme, Replicates	5 @ Level 1 2 @ Levels 2 & 5 3 @ Levels 4 & 6
Calibration Frequency:	Every new reagent cartridge lot Every 90 days for any one lot For each new lot of Flex reagent cartridges After major maintenance or service, if indicated by quality control results As indicated in laboratory quality control procedures When required by government regulations
Assigned Coefficients:	C0 -1000.0 C1 3000.0 C2 -2.0 C3 200.0 C4 0.5

INTERPRETATION:
The instrument automatically calculates and prints the concentration of PSA in ng/mL [µg/L].

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

LIMITATIONS:

Results: >100 ng/mL [µg/L]

Manual dilution: Make appropriate dilution with Reagent Grade Water to obtain results within assay range. Enter dilution factor. Reassay. Resulting readout is corrected by dilution.

Autodilution: Refer to your Dimension® system manual.

Results: <0.13 ng/mL [µg/L] should be reported as less than 0.13 ng/mL [µg/L].

PSA levels may be lower in patients who receive hormonal therapy and may not adequately reflect the presence of residual or recurrent disease.[15]

Patient samples may contain heterophilic antibodies that could react in immunoassays to give falsely elevated or depressed results. This assay has been designed to minimize interference from heterophilic antibodies.[17]

The instrument reporting system contains error messages to warn the operator of specific malfunctions. Any report slip containing such error messages should be held for follow-up. Refer to your Dimension® system manual.

Expected Values:

0.0-4.0 ng/ml

REPORTING:
report format: ng/ml

ANALYTICAL SPECIFICITY:

For Known Interfering Substances section refer to package insert.

For Known Non-Interfering Substance refer to package insert.

For Additional Technical Information refer to package insert.

Reference: PSA Flex® reagent cartridge insert sheet PN 755450.001 Issue Date 2015-04-08

Origination Date: 9-10-07
Date of Implementation: 11-10-10
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Written By: ____Lori Murray MT(ASCP)_____ Date: _8-10-12_____

Approved By: __Aaron Shives, MD___ Date: __10/23/2017___
Laboratory Director

REVIEW - REVISION SUMMARY DOCUMENTATION

Date	By	Revision Summary
07/10	Lori Murray	New format
12-21-10	Lori Murray	change in lowest reportable value
8-12	Lori Murray	Change instrumentation to EXL200
5/15/15	Heather Hall	Updated information to package insert dated 3/1/2011
8/26/15	Amy Harms	Updated information Risk and Safety dated 2015/4/08
10/17/15	Heather Hall	Updated link to SDS, modified backup process