TRAINING UPDATE

Lab Location:	SGMC	**Date Distributed:**	8/15/2017
Department:	Core Lab	**Due Date:**	8/31/2017
		Implementation:	**8/31/2017**

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:

PSA Total by Dimension Vista® System SGAH.C916 v1

Description of change(s):

(note QC change is already in effect)

Section	Reason
3.2	Remove specimen onboard stability
4,5,6	Remove individual section labeling instructions and add general one
6.1, 6.2	Update QC material and storage
7.2	Change freezer upper limit to -50C
10.5	Move patient review from section 6
10.6	Remove repeat value below AMR/CRR *
11.3	Move report comment from 10.6
15	Update to new standard wording, add reagent hazard warnings
17	Update QC product and PI dates

* This change will be made to Vista assays as SOPs are revised

This revised SOP will be implemented on August 31, 2017

Document your compliance with this training update by taking the quiz in the MTS system.

Technical SOP

Title	**PSA Total by Dimension Vista® System**	
Prepared by	Ashkan Chini	Date: 5/8/2015
Owner	Robert SanLuis	Date: 5/8/2015

Laboratory Approval	**Local Effective Date:**	
Print Name and Title	**Signature**	**Date**
Refer to the electronic signature page for approval and approval dates.		

Review		
Print Name	**Signature**	**Date**

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TABLE OF CONTENTS

1. TEST INFORMATION

Assay	Method/Instrument	Local Code
PSA Total	Dimension Vista® System	PSAT

Synonyms/Abbreviations
PSA, Prostatic Antigen, Prostate-Specific Antigen, TPSA

Department
Chemistry

2. ANALYTICAL PRINCIPLE

The TPSA method is a homogeneous, sandwich chemiluminescent immunoassay based on LOCI technology. The LOCI reagents include two synthetic bead reagents and a biotinylated anti-TPSA monoclonal antibody F(ab') fragment. The first bead reagent (Chemibeads) is coated with anti-TPSA monoclonal antibody and contains chemiluminescent dye; the second bead reagent (Sensibeads) is coated with streptavidin and contains a photosensitizer dye. Sample is incubated with biotinylated antibody and Chemibeads to form bead/TPSA/biotinylated antibody sandwiches. Sensibeads are then added and bind to the biotin to form bead pair immunocomplexes. When illuminated by light at 680 nm, Sensibeads convert dissolved oxygen in the reaction solution into singlet oxygen form. In the bead pairs, the singlet oxygen diffuses ("channels") into Chemibeads, triggering a chemiluminescent reaction. The resulting chemiluminescent signal is measured at 612 nm and is directly proportional the concentration of TPSA in the sample.

3. SPECIMEN REQUIREMENTS

3.1 Patient Preparation

Component	Special Notations
Fasting/Special Diets	N/A
Specimen Collection and/or Timing	Normal procedures for collecting and storing serum and plasma may be used for samples to be analyzed by this method.
Special Collection Procedures	N/A
Other	N/A

3.2 Specimen Type & Handling

Criteria		
Type -Preferred **-Other Acceptable**	Plasma (Lithium Heparin) Serum	
Collection Container	Plasma: Mint green top tube (PST) Serum: Red top tube, Serum separator tube (SST)	
Volume - Optimum **- Minimum**	1.0 mL 0.5 mL	
Transport Container and Temperature	Collection container or Plastic vial at room temperature	
Stability & Storage Requirements	Room Temperature:	8 hours*
	Refrigerated:	24 hours*
	Frozen:	7 days*

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Criteria	
Timing Considerations	Serum or plasma should be physically separated from cells as soon as possible with a maximum limit of four hours from the time of collection.
Unacceptable Specimens & Actions to Take	Specimens that are unlabeled, improperly labeled, or those that do not meet the stated criteria are unacceptable. Request a recollection and credit the test with the appropriate LIS English text code for "test not performed" message. Examples: Quantity not sufficient-QNS; Wrong collection-UNAC. Document the request for recollection in the LIS.
Compromising Physical Characteristics	Gross hemolysis. Reject sample and request a recollection. Credit the test with the appropriate LIS English text code explanation of HMT (Specimen markedly hemolyzed)
Other Considerations	Allow Red Top or SST to clot completely prior to centrifugation.

*This information does not match Siemens Package Insert. It is based on the validation which is performed internally in this laboratory. Validation information is available for review.

NOTE: Labeling requirements for all reagents, calibrators and controls include: (1) Open date, (2) Substance name, (3) Lot number, (4) Date of preparation, (5) Expiration date, (6) Initials of tech, and (7) Any special storage instructions. Check all for visible signs of degradation. When placed onboard the analyzer, the instrument captures the date / time loaded and calculates and tracks the opened expiration.

4. REAGENTS

The package insert for a new lot of kits must be reviewed for any changes before the kit is used. A current Package Insert is included as a Related Document.

4.1 Reagent Summary

Reagents	Supplier & Catalog Number
TPSA	Siemens, Flex® reagent cartridge, Cat. No. K6451

4.2 Reagent Preparation and Storage

Reagent	**TPSA**
Container	Reagent Cartridge
Storage	Store at 2-8° C
Stability	• Stable until expiration date stamped on reagent cartridges. • Sealed wells on the instrument are stable for 30 days. • Once wells 1 - 12 have been entered by the instrument, they are stable for 5 days.
Preparation	All reagents are liquid and ready to use.

5. CALIBRATORS/STANDARDS

5.1 Calibrators/Standards Used

Calibrator	Supplier and Catalog Number
PSA CAL	Siemens Dimension Vista®, Cat. No. KC602

5.2 Calibrator Preparation and Storage

Calibrator	PSA CAL
Preparation	Calibrator is ready for use. No preparation is required.
Storage/Stability	• Store at 2-8°C • **Unopened calibrator** is stable until expiration date stamped on the box. • **Opened Calibrator:** once the stopper of the vial is punctured, assigned values are stable for 7 days when stored on board the Dimension Vista System.

5.3 Calibration Parameter

Criteria	Special Notations
Reference Material	PSA CAL
Assay Range	0.1 – 100.0 ng/mL
Suggested Calibration Level	See Reagent Package Insert for lot specific assigned values in ng/mL
Frequency	• Every new reagent cartridge lot. • Every 30 days for any one lot • When major maintenance is performed on the analyzer. • When control data indicates a significant shift in assay.
Calibration Scheme	6 Levels, n = 3

5.4 Calibration Procedure

Auto Calibration:

1. Place the required calibrator vials in a carrier. Make sure the barcode labels are entirely visible through the slots.
2. Place the carrier in the loading area.
3. Position the carrier with the labels facing away from the user.
4. Press the **Load** button.
5. Automatic calibration requires that calibrators be on the instrument. As the time for processing approaches, the instrument reviews onboard inventory for the appropriate calibrators.

Manual Calibration:

1. Verify that calibrators and reagents are in inventory on the instrument.
2. Press **System > Method Summary > Calibration**.
3. Select a method from the sidebar menu. Press the **Order Calibration** button on the screen.
4. Verify that the information on the screen is correct. Verify that the calibrator lot is correct using the drop-down menu.
   a. When calibrating using Vials press **OK**.
   b. When calibrating using Cups, check the Use Cups box. This displays the rack and cup position fields. For additional cups use the positions in ascending order. Be sure to use the number of calibration levels and cups as specified in the method IFU. Scan the rack barcode and place calibrator cups in an adapter in position 1 on a rack. Press **OK** and load the rack on the instrument.
5. The status field in the calibration screen changes sequentially to Awaiting Scheduling, Preparing Calibrators and Processing.

5.5 Tolerance Limits

IF……	THEN……
If result fall within assay-specific specification, and QC values are within acceptable limits,	proceed with analysis
If result falls outside assay-specific specification, or QC values are out of Acceptable limits,	troubleshoot the assay and/or instrument and repeat calibration

6. QUALITY CONTROL

6.1 Controls Used

Controls	Supplier and Catalog Number
Liquichek Immunoassay Plus Control Levels 1, 2 and 3	Bio-Rad Laboratories Cat. No. 267, 268 and 269

6.2 Control Preparation and Storage

Control	Immunoassay Plus Control Levels 1, 2 and 3
Preparation	Allow the vials to stand at room temperature (18-25°C) until it is completely thawed. Gently swirl the vial several times to ensure homogeneity and immediately load on instrument. After each use, promptly replace the stopper and return to 2-8°C storage.
Storage/Stability	Once the control is thawed, all analytes will be stable for 4 days at 2-8°C. Unthawed controls are stable until the expiration date at -20 to -50°C.

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6.3 Frequency

Analyze all levels of QC material after every calibration and each day of testing (notated on the QC frequency sheets posted on the instruments).

Refer to the Dimension Vista® QC Schedule in the Laboratory policy Quality Control Program and in the Dimension Vista® Quick Reference Guide.

6.4 Tolerance Limits and Criteria for Acceptable QC

Step	Action
1	Acceptable ranges for QC are programmed into the instrument's Quality Control software system and Unity Real Time, and may be posted near the instrument for use during computer downtime.
2	**Run Rejection Criteria** • Anytime the established parameters are exceeded (if one QC result exceeds 2 SD), the run is considered out of control (failed) and patient results must not be reported. • The technologist must follow the procedure in the Laboratory QC Program to resolve the problem.
3	**Corrective Action**: • All rejected runs must be effectively addressed through corrective action. Steps taken in response to QC failures must be documented. Patient samples in failed analytical runs must be reanalyzed according to the Laboratory QC Program. Supervisors may override rejection of partial or complete runs only with detailed documentation and criteria for overrides that are approved by the Medical Director. Consult corrective action guidelines in Laboratory QC Program. Follow corrective action guidelines in the Laboratory QC Program. • Corrective action documentation must follow the Laboratory Quality Control Program.
4	**Review of QC** • QC must be reviewed weekly by the Group Lead or designee and monthly by the Supervisor/Manager or designee. • If the SD and/or CV are greater than established ranges, investigate the cause for the imprecision and document implementation of corrective actions.

6.5 Documentation

- QC tolerance limits are programmed into the instrument and Unity Real Time; it calculates cumulative mean, SD and CV and stores all information for easy retrieval.

- Quality control records are reviewed daily at the bench, weekly by the Group Lead or designee, and monthly by the Supervisor/Manager or designee.
- Refer to complete policies and procedures for QC documentation and for record retention requirements in the Laboratory QC Program.

6.6 Quality Assurance Program

- Each new lot number of reagent or new shipment of the same lot of reagent must be tested with external control materials and previously analyzed samples. Performance of the new lot must be equivalent to the previous lot; utilize published TEA for acceptability criteria.
- Training must be successfully completed and documented prior to performing this test. This procedure must be incorporated into the departmental competency assessment program.
- The laboratory participates in CAP proficiency testing. All proficiency testing materials must be treated in the same manner as patient samples.
- Monthly QC must be presented to the Medical Director or designee for review and signature.
- Monthly QC mean and SD are sent to Bio-Rad Laboratories for peer group comparison.
- Consult the Laboratory QC Program for complete details.

7. EQUIPMENT and SUPPLIES

7.1 Assay Platform

Dimension Vista® System

7.2 Equipment

- Refrigerator capable of sustaining 2–8°C.
- Freezer capable of sustaining range not to exceed -20 to -50°C.
- Centrifuge

7.3 Supplies

- Aliquot Plates
- System Fluids
- Assorted calibrated pipettes (MLA or equivalent) and disposable tips

8. PROCEDURE

TPSA Flex® reagent cartridge Cat. No. K6451 is required to perform this test.

TPSA is performed on the Dimension Vista® System after the method is calibrated (see Reference Material in Calibration section) and Quality Controls are acceptable.

NOTE: For all procedures involving specimens, buttoned lab coats, gloves, and face protection are required minimum personal protective equipment. Report all accidents to your supervisor.

8.1	Sample Processing
1.	A sample rack holding tubes or cups is placed on the rack input lane.
2.	The sample shuttle moves the rack to the barcode reader which identifies the rack and samples to the system.
3.	The rack moves into the sample server and to the rack positioner.
4.	At the same time, aliquot plates move from the aliquot loader into position.
5.	The aliquot probe aspirates the sample from the tubes or cups and dispenses it into the wells of the aliquot plates.
6.	After each aspirate-dispense action, the probe is thoroughly rinsed inside and out to prevent sample carryover.
7.	When sample aspiration is completed, the sample server moves the rack back to the sample shuttle, where it is placed on the output lane and can be removed by the operator.

8.2	Specimen Testing
1.	For QC placement and frequency, refer to the Dimension Vista® QC Schedule in the Laboratory QC Program.
2.	Follow the instructions, outlined in the Dimension Vista® Operator's Manual
3.	The instrument reporting system contains error messages to warn the user of specific malfunctions. Results followed by such error messages should be held for follow-up. Refer to the Dimension Vista® system manual "Error messages" section for troubleshooting.
4.	Follow protocol in Section 10.5 "Repeat criteria and resulting" for samples with results above or below the Analytical Measurement Range (AMR). Investigate any failed delta result and repeat, if necessary.
5.	Append the appropriate English text code qualifier messages to any samples requiring a comment regarding sample quality and/or any other pertinent factors.

Test Conditions	
Sample Volume:	3 µL
Biotinylated Antibody Reagent Volume:	20 µL
Chemibead Reagent Volume:	20 µL
Streptavidin Sensibead Reagent Volume:	100 µL
Reaction Time:	10 minutes
Test Temperature:	37°C
Wavelength:	680 & 612
Type of measurement:	Chemiluminescence

9. CALCULATIONS

The instrument automatically calculates the concentration of PSA Total in ng/mL.

10. REPORTING RESULTS AND REPEAT CRITERIA

10.1 Interpretation of Data

None required

10.2 Rounding

Instrument reports results with one decimal point.

10.3 Units of Measure

ng/mL

10.4 Clinically Reportable Range (CRR)

0.1 – 10,000.0 ng/mL

10.5 Review Patient Data

Each result is reviewed for error messages. Refer to the Dimension Vista system manual "Error messages" section for troubleshooting. Resolve any problems noted before issuing patient reports.

10.6 Repeat Criteria and Resulting

All repeats must replicate the original result within the total allowable error (TEa) of the assay. Refer to TEa listing for specific information.

Values that fall below or within the AMR or CRR may be reported without repeat. Values that exceed ~~fall outside~~ the upper ranges must be repeated.

IF the result is …	THEN…
< 0.1 ng/mL	Assure there is sufficient sample devoid of bubbles, cellular debris, and/or fibrin clots. Report as: < 0.1 ng/mL
≥ 100.0 ng/mL	**On Board Automated Dilution:** Results ≥ 100.0 ng/mL will automatically have repeat testing performed into the instrument using dilution factor of 20. No multiplication is necessary.

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IF the result is …	THEN…
> 2,000.0 ng/mL	**Manual Dilution:** Using the primary tube, make the smallest dilution possible to bring the raw data within the AMR. Maximum allowable dilution: x 100 **Diluent:** Reagent Grade Water Enter dilution factor as a whole number on the "Enter Sample Data" screen.
> 10,000.0 ng/mL	If the recommended dilution does not give results within the clinically reportable range, report as: "> 10,000.0 ng/mL-REP" Bring to the attention of you supervisor prior to releasing result.

Message	Code
Verified by repeat analysis	Append –REP to the result.

11. EXPECTED VALUES

11.1 Reference Ranges

< 4.0 ng/mL

11.2 Critical Values

None established

11.3 Standard Required Messages

The following comment is automatically added to the report by the LIS:

"This test was performed using the Siemens Dimension Vista Chemiluminescence method. Values obtained from different assay methods cannot be used interchangeably. PSA levels, regardless of value, should not be interpreted as absolute evidence of the presence or absence of disease."

12. CLINICAL SIGNIFICANCE

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.
In serum PSA exists primarily as three forms: free and complexed with either a1-antichymotrypsin (ACT) or a2-macroglobulin. The PSA protein associated with a2-macroglobulin is encapsulated and unavailable for measurement by current immunoassay systems. The TPSA assay on the Dimension Vista System measures both the free and the ACT bound components of serum PSA equally, a property known as equimolarity.

The specificity of PSA to prostate tissue makes it a significant marker as an aid to 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. Prior to the use of PSA for early detection of prostate cancer, the traditional method of digital rectal examination (DRE) detected considerably fewer tumors. 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 or 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 an adjunctive test in the management of prostate cancer. 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 non-detectable level. A rise of the serum PSA level in prostatectomy patients indicates residual prostate tissue; recurrence or metastasis of the disease. Serum PSA levels during radiation treatment should decline and remain at baseline while the patient is in remission.

13. PROCEDURE NOTES

- **FDA Status:** FDA Approved/modified
- **Validated Test Modifications:** Specimen stabilities have been modified from the package insert based on in-house stability studies performed at Shady Grove Medical Center.

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 Vista Operator's Guide.

The expected maximum observed standard deviations for repeatability using n = 5 replicates at the following TPSA concentrations are:

TPSA Concentration	Acceptable S.D. Maximum
4 ng/mL	0.22 ng/mL
20 ng/mL	1.21 ng/mL

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

0.1 – 100.0 ng/mL

14.2 Precision

Material	Mean ng/mL	Standard Deviation (%CV)	
		Repeatability	Within-Lab
Serum Pool	0.46	0.013	0.24
Liquichek 1	2.33	0.03	0.07
Liquimmune	14.6	0.21	0.34

14.3 Interfering Substances

An erroneously elevated PSA Total level can be observed if the serum specimen from a patient is collected following digital rectal examination, needle biopsy or transurethral resection.

HIL Interference:
The TPSA method was evaluated for interference according to CLSI/NCCLS EP7-A2. Bias, defined as the difference between the control sample (does not contain interferent) and the test sample (contains interferent), is shown in the table below. Bias exceeding 10% is considered "interference".

Substance tested	Substance Concentration	TPSA ng/mL	Bias %
Hemoglobin (hemolysate)	500 mg/dL	N/A	<10
Bilirubin (unconjugated)	20 mg/dL	N/A	<10
Bilirubin (conjugated)	20 mg/dL	N/A	<10
Lipemia Intralipid®	3000 mg/dL	N/A	<10

14.4 Clinical Sensitivity/Specificity/Predictive Values

Not available

15. SAFETY

Refer to your local and corporate safety manuals and Safety Data Sheet (SDS) for detailed information on safety practices and procedures and a complete description of hazards.

TPSA Flex® Reagent Cartridge and PSA CAL may cause an allergic skin reaction. Contain 5-chloro-2-methyl-3(2h)-isothiazolone mixture with 2-methyl-3(2h)-isothiazolone. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention.

16. RELATED DOCUMENTS

1. Dimension Vista® Clinical Chemistry System Operator's Manual
2. Dimension Vista® Calibration/Verification Procedure
3. Dimension Vista® Cal Accept Guidelines
4. Dimension Vista® Calibration summary
5. Dimension Vista® Sample Processing, Startup and Maintenance procedure

6. Laboratory Quality Control Program
7. QC Schedule for Siemens Dimension Vista®
8. Laboratory Safety Manual
9. Safety Data Sheets (SDS)
10. Dimension Vista® Limits Chart (AG.F200)
11. Quest Diagnostics Records Management Procedure
12. Dimension Vista® System Error Messages Chart
13. Centrifuge Use, Maintenance and Functions Checks (Lab policy)
14. Hemolysis, Icteria and Lipemia Interference (Lab policy)
15. Repeat Testing Requirement (Lab policy)
16. Current Allowable Total Error Specifications at http://questnet1.qdx.com/Business_Groups/Medical/qc/docs/qc_bpt_tea.xls
17. Current package insert TPSA Flex® Reagent Cartridge K6451

17. REFERENCES

1. Package Insert, TPSA Flex® Reagent Cartridge K6451, Siemens Healthcare Diagnostics Inc., 6/10/2016
2. Package Insert, PSA CAL, Siemens Healthcare Diagnostics Inc., 6/2016.
3. Package Insert, Liquichek Immunoassay Plus Control, Bio-Rad Laboratories, revised 12/2015.
4. PSA by Siemens Centaur SOP from Quest Diagnostics Nichols Institute in Chantilly, VA. Document CHA QDIC747 v1.0H

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval
0	7/26/17	3.2	Remove specimen onboard stability	L Barrett	R SanLuis
0	7/26/17	4,5,6	Remove individual section labeling instructions and add general one	L Barrett	R SanLuis
0	7/26/17	6.1, 6.2	Update QC material and storage	L Barrett	R SanLuis
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0	7/26/17	15	Update to new standard wording, add reagent hazard warnings	L Barrett	R SanLuis
0	7/26/17	17	Update QC product and PI dates	L Barrett	R SanLuis

19. ADDENDA

None