CPAL
Central **P**ennsylvania **A**lliance **L**aboratory

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Free PSA
- New Assay -

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Ordering Information:

Mnemonics:	**PSA Group**	**PSA Reflex**
Test Name:	**PSA Group**	**PSA Reflex**
Test Number:	1750049	1750050
Includes	Total PSA, Free PSA, and % Free PSA	Total PSA: If Total PSA is 4-10 ng/ml, Free PSA and % Free PSA are added.
Specimen:	Specimen: Serum- Special handling- Spin and refrigerate specimen within 3 hours of collection. Stable 24 hours refrigerated.	

Effective Date: Testing offered beginning on Monday, November 16, 2015.

Performed: Monday through Saturday

Reference Range: >25% free PSA for total PSA between 4 and 10 ng/mL

Background:
Prostate cancer is the most common type of cancer found in men in the United States, with an incidence of approximately one case for every ten men. It is also the second leading cause of cancer deaths among American men.

PSA, a serine protease, is produced by the epithelial cells of the prostate, and is produced by both benign and malignant cells. Abnormalities in the prostate gland architecture resulting from trauma or disease can lead to "leakage" of PSA into the bloodstream. PSA exists primarily as three forms in serum. One form of PSA is believed to be enveloped by the protease inhibitor, alpha-2 macroglobulin and has been shown to lack immunoreactivity. A second form is complexed to another protease inhibitor, alpha-1 antichymotrypsin (ACT). The third form of PSA is not complexed to a protease inhibitor, and is termed free PSA. The latter two forms are immunologically detectable in commercially available PSA assays and are referred to collectively as total PSA.

Measurement of PSA forms is useful in the differentiation of prostate cancer from benign prostatic conditions. In patients with elevated PSA concentrations, men with prostate cancer tend to have lower percent free PSA (free PSA/total PSA) values than men with benign disease. This difference in the distribution of percent free PSA values in men with and without cancer may be used to select cutoffs for biopsy decisions, maintaining 90% to 95% sensitivity, while sparing 20% to 30% of men with benign disease from biopsy. Percent free PSA may also be used for risk assessment, to determine the probability of cancer for an individual patient. Lower percent free PSA values are associated with higher risk of cancer.

Principle of Test:
Access Hybritech free PSA is intended to be used with Hybritech (total) PSA to calculate the ratio of free PSA to total PSA expressed as a percentage (percent free PSA). Percent free PSA as measured by the Hybritech assays is indicated for use as an aid in distinguishing prostate cancer from benign prostatic conditions, when used in conjunction with Hybritech (total) PSA for prostate cancer detection in men aged 50 years and older with total PSA between 4 and 10 ng/mL with digital rectal examination findings that are not suspicious for cancer. Prostatic biopsy is required for diagnosis of cancer.

The Access Hybritech free PSA assay is a paramagnetic particle, two-site immunoenzymatic ("sandwich") chemiluminescent immunoassay for the quantitative determination of free prostate specific antigen (free PSA) in human serum using the Access Immunoassay Systems.

Results Interpretation:
Percent free PSA may be used to determine the relative risk of prostate cancer in individual men. Family and patient history can be used in combination with percent free PSA results to determine the best individualized patient management decisions.

Figure 1.0 shows the probability of detecting prostate cancer with needle biopsy, based on total PSA and percent free PSA results. PSA results in this table were obtained from a prior multi-center study evaluating the efficacy of total PSA for prostate cancer detection, and percent free PSA results were obtained from the current study. It can be seen that rising PSA levels increase the risk of detectable cancer. Percent free PSA can further stratify risk for men with PSA values between 4 ng/mL and 10 ng/mL and non-suspicious digital rectal examination results. Lower percent free PSA values indicate higher risk. The risk of cancer ranged from 8% to 56% for this population. For purposes of comparison, the risk of prostate cancer is 4% for the general population of men over 50 years of age.

Figure 1.0 Probability of Prostate Cancer, Based on PSA and Percent free PSA Results (For Men with Non-Suspicious DRE Results, Regardless of Patient Age)

PSA (Hybritech Calibration)	PSA (WHO Calibration)	Probability of Cancer
0–2 ng/mL	0–1.6 ng/mL	1%
2–4 ng/mL	1.6–3.1 ng/mL	15%
4–10 ng/mL	3.1–7.8 ng/mL	25%
> 10 ng/mL	> 7.8 ng/mL	> 50%

Percent free PSA	Probability of Cancer
0–10%	56%
10–15%	28%
15–20%	20%
20–25%	16%
> 25%	8%

Single Cutoff
Rather than using risk assessment, a cutoff approach to patient management can also be used. A cutoff of ≤ 25% free PSA was selected based on data from the clinical trial. When men with values of 25% free PSA or less were biopsied, 95% of cancers were detected. The majority of men with PSA values between 4 ng/mL and 10 ng/mL have benign disease. In this clinical trial, 20% of biopsied men with benign disease and a percent free PSA value greater than the 25% free PSA cut-off could have been spared from biopsy. The cutoff of ≤ 25% free PSA is based on results from this clinical trial. Additional follow-up may be recommended for men with percent free PSA values above 25%, if the physician believes it is necessary based upon other factors in the patient's medical or family history.

Limitations:
1. As for all assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g. HAMA, that interfere with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples. Such interfering antibodies may cause erroneous results. Carefully evaluate the results of patients suspected of having these antibodies.

2. The Access Hybritech free PSA results should be interpreted in light of the total clinical presentation of the patient, including: symptoms, clinical history, data from additional tests, and other appropriate information. Serum PSA concentrations (free, total, or percent free PSA) should not be interpreted as absolute evidence for the presence or absence of prostate cancer. Elevated total PSA concentrations or decreased percent free PSA may be observed in the serum of patients with non-malignant disorders, as well as those with prostate cancer. Low total PSA concentrations or elevated percent free PSA are not necessarily indicative of the absence of cancer.
3. Serum free and total PSA values should be used in conjunction with information available from the clinical evaluation of the patient and other diagnostic procedures such as digital rectal examination (DRE). Some cases of early prostate cancer will not be detected by PSA testing; the same is true for DRE. Biopsy of the prostate is the standard method used to confirm the presence or absence of prostate cancer.
4. The Access Hybritech free PSA assay does not demonstrate any "hook" effect up to 20,000 ng/mL with Hybritech calibration or 15,800 ng/mL with WHO calibration.
5. The 5 alpha-reductase inhibitor drugs may affect PSA levels in some patients. Other drugs used to treat benign prostatic hyperplasia (BPH) may also affect PSA levels. Care should be taken in interpreting results from patients taking these drugs.
6. Free PSA concentrations are dependent on the standard used to calibrate the assay. Free PSA concentrations based on calibration to the WHO 96/668 Reference Preparation will differ significantly from free PSA concentrations based on calibration to the original Hybritech Tandem-R assay. The concentrations are not interchangeable.
7. This test was performed using the Beckman Coulter Immunoassay method. Values obtained from different methods cannot be used interchangeably. PSA levels, regardless of value, should not be interpreted as absolute evidence of the presence or absence of disease.

Validation Data:

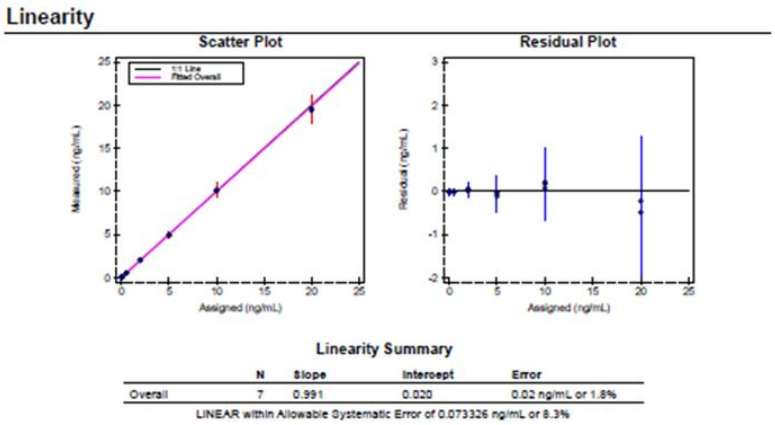
For within run precision, two levels of control were run ten times each, within the same run, on all 4 pipettors. For between run precision, two levels of control were run five times each on two different days. The %CVs fall within the Manufacturer's claim of <7%. **(**Table 1)

Table 1: Precision

Within Run Precision				Between Run Precision			
Mean Lev 1	**CV**	**Mean Lev 3**	**CV**	**Mean Lev 1**	**CV**	**Mean Lev 3**	**CV**
0.268 ng/mL	3.7%	17.031	2.8%	0.264 ng/mL	2.7%	16.928	3.7%

Linearity/Analytical Measurement Range:

To verify the analytical measurement range (AMR) of the assay, free PSA calibrators of a different lot than those used to calibrate the assay, were run in triplicate. To verify the lower end of linearity, the S1 calibrator was diluted with the S0 calibrator at 1:10. The assay is linear within Allowable Systematic Error of 0.073326 ng/mL or 8.3%, covering the AMR of 0.01 – 20.0 ng/mL.

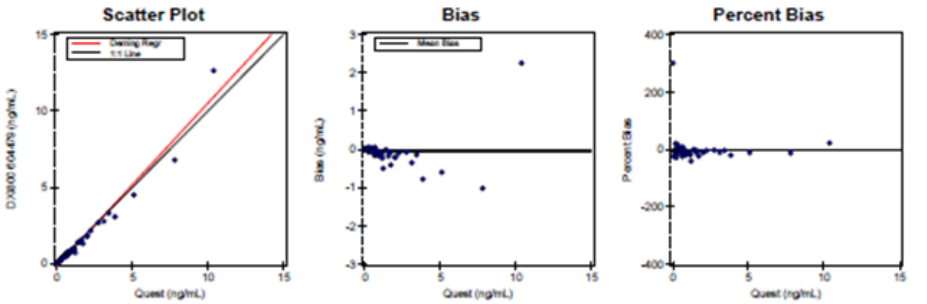


Method Correlation validation

A total of 41 specimens were split and processed utilizing the Access Hybritech free PSA assay and % free PSA versus results from Quest Diagnostics.

Free PSA Method Comparison:

X Method Quest Y Method DXI800 604479



Regression Analysis

	Deming	Passing-Bablok	Regular
Slope	1.069 (1.010 to 1.128)	0.897 (0.870 to 0.944)	1.048 (0.990 to 1.107)
Intercept	-0.172 (-0.313 to -0.032)	0.014 (-0.004 to 0.036)	-0.144 (-0.284 to -0.004)
Std Err Est	0.395	--	0.393

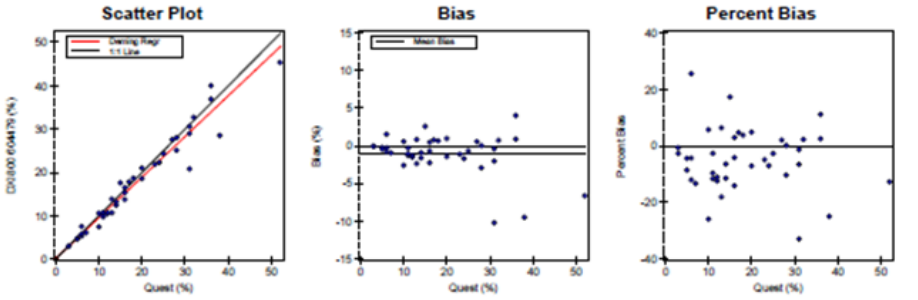
95% Confidence Intervals are shown in parentheses

Supporting Statistics

Corr Coef (R)	0.9822	SubRange Bounds	None
Bias	-0.076 (-5.600 %)	Points (Plotted/Total)	49/50
X Mean ± SD	1.397 ± 1.940	Outliers	Not Tested
Y Mean ± SD	1.321 ± 2.071	Scatter Plot Bounds	None
Std Dev Diffs	0.400		

% Free PSA Method Comparison:

X Method Quest Y Method DXI800 604479



Regression Analysis

	Deming	Passing-Bablok	Regular
Slope	0.939 (0.868 to 1.010)	0.983 (0.921 to 1.045)	0.915 (0.845 to 0.985)
Intercept	0.136 (-1.382 to 1.655)	-0.344 (-1.245 to 0.217)	0.573 (-0.936 to 2.082)
Std Err Est	2.496	--	2.481

95% Confidence Intervals are shown in parentheses

Supporting Statistics

Corr Coef (R)	0.9730	SubRange Bounds	None
Bias	-0.985 (-5.518 %)	Points (Plotted/Total)	41/41
X Mean ± SD	18.341 ± 11.284	Outliers	Not Tested
Y Mean ± SD	17.357 ± 10.612	Scatter Plot Bounds	None
Std Dev Diffs	2.631		

Suggested CPT Codes: Free PSA-84154. No CPT code for % free PSA.

References:

1. Beckman Coulter Access Hybritech free PSA Assay Instructions For Use, June 2015.
2. Beckman Coulter Access Hybritech free PSA Calibrators Instructions For Use, May 2015.