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

Technical Bulletin

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Prostate Specific Antibody (PSA)
- METHOD CHANGE –

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Effective Date:

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Method Change:

Due to an Urgent Medical Device Recall of PSA reagents by Siemens received on June 27, 2013 and the lack of available replacement reagents for the Siemens Immulite 2000 system, PSA testing was changed to the Hybritech calibration method on the Beckman-Coulter DxI800. A comment included with each PSA result reflects this change.

In the recall notice, Siemens described an overall average positive bias of approximately 20-23% relative to WHO 96/670. The product recall included 20 lots of reagents, some of which were in use at CPAL beginning in May of 2012

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. A reliable test for detecting early stage prostate cancer, when the tumor is confined to the gland and effective treatment can be provided, can be of great value to the physician. Historically, a majority of prostate cancers had advanced beyond the gland at the time of diagnosis. The digital rectal examination (DRE) is a commonly used technique for prostate cancer detection; nevertheless DRE, as it is generally performed in medical practice, misses a significant number of cancers, including many organ-confined tumors.

Prostate specific antigen (PSA) was identified and purified by Wang and co-workers in 1979. PSA is a single chain glycoprotein with a molecular weight of approximately 34,000 daltons, containing 7% carbohydrate by weight. 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. The relative concentrations of the two detectable forms within and between patient samples is variable and unknown. However, it has been reported that the concentration of free PSA usually ranges from 5 to 50% of the total PSA in serum. Additional studies have also shown that various immunoassays react differently to these two forms in serum. Specifically, there are two distinct types of immunoassays, based upon their relative response to PSA forms. Equimolar-response assays detect the free and complexed forms of PSA equally; non-equimolar or skewed-response assays have been shown to produce two to three times more signal per free PSA molecule than with PSA-ACT. The Access Hybritech PSA assay is an equimolar assay in which sample recovery is unaffected by the ratio of PSA forms in serum. Therefore, the reported result is not changed by the relative concentrations of free PSA and PSA-ACT in the sample. Results generated by the Access Hybritech PSA assay cannot be applied to other manufacturers' assays.

Elevated serum PSA concentration can only suggest the presence of prostate cancer until a biopsy is performed. Serum PSA concentrations can also be elevated in benign prostatic hypertrophy or inflammatory conditions of the prostate and other adjacent tissues. PSA is generally not elevated in apparently healthy men or men with non-prostatic carcinoma. Physicians should discuss the risks and benefits of PSA testing with their patients.

Supporting Data:

A total of 70 patient samples were tested at CPAL by the Siemens Immulite 2000 and Beckman-Coulter DxI800 methods. Figure 1 shows the overall patient correlation, with samples ranging from none detected to 1512 ng/dL. Figure 2 shows the lower range of specimens expanded to show specimens between none detected and 46.4 ng/dL. Figures 3 and 4 show absolute and % bias respectively. There was an overall negative bias of 27.8% on the DxI800, as compared with the Immulite 2000.

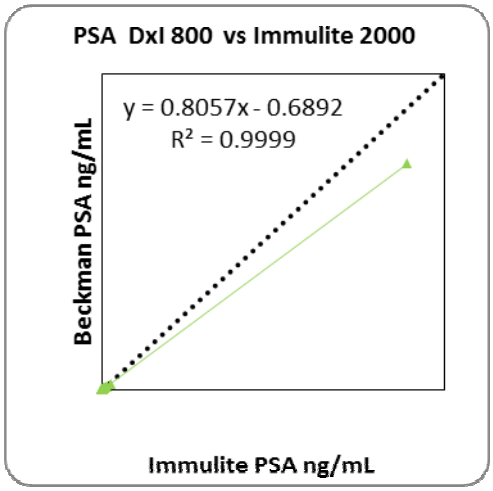

Figure 1: Patient Correlation

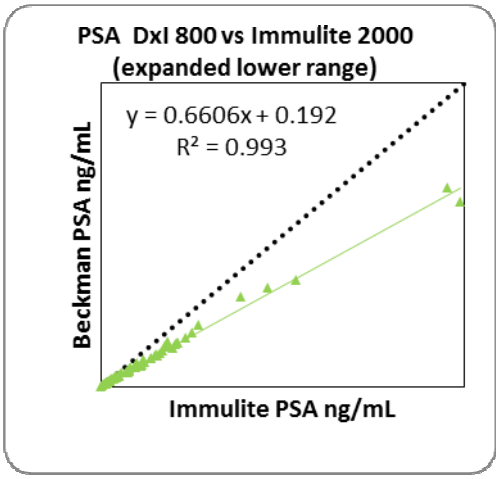

Figure 2: Patient Correlation 0-50 ng/dL

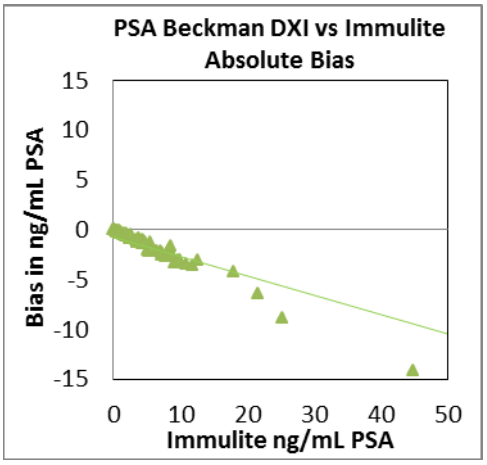

Figure 3: Absolute Bias

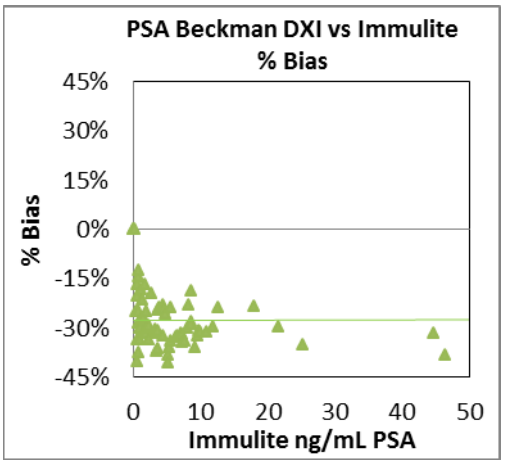

Figure 4: % Bias

Reference Ranges:

Since the references ranges were set prior to the current reported Immulite positive bias and reference ranges for this assay are generally literature based, there will be no change in the reference ranges.

Risk to Health:

In the notice of Urgent Medical Device Recall, Siemens states the following as to health risk and need for look back:

"A positive bias in the PSA results may impact clinical interpretation of test results. In cases where the true values are near the cut off, the bias may increase the likelihood of a decision to initiate additional diagnostic tests (including prostatic biopsy). The risk of unnecessary biopsy is mitigated by the fact that the clinician/patient decision for prostatic biopsy is based on a number of factors in addition to a PSA result, including patient age, digital rectal exam findings, clinical signs or symptoms or co morbidities such as prostatic inflammation or infection."

Look Back:

Further, the notice made recommendations as to the look back period as follows:

"The decision to perform a biopsy is usually undertaken within a short period of time from the assay result. Therefore a conservative look back period can be limited to two months of test results. For results that were recorded as abnormal in your facility please notify your physicians of this communication. Actions by the clinician may be to reconsider a scheduled biopsy based on the test result taking into account the other factors that made biopsy a consideration. **Clinical decisions are the responsibility of the patient's caregiver. The positive bias does not negate the necessity of a biopsy if other findings support the decision.**"

CPAL is providing the ordering institution **ALL** affected results obtained with the affected lots of reagent. This includes results dating back to May 2012. We suggest that all physicians for patients affected be notified of the recall.

Baseline Values for Affected Patients:

Since no replacement reagents are available for the Immulite 2000, CPAL is unable to provide parallel testing to re-baseline patients.