IMPROVED SENSITIVITY ON THE BECKMAN COULTER DxI 9000 IMMUNOASSAY ANALYZER* ENABLES REDUCTION OF REQUIRED SAMPLE AND REAGENT VOLUMES FOR IMMUNOASSAYS

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B-005

BACKGROUND

The Beckman Coulter DxI 9000 analyzer includes new technology that improves assay sensitivity capabilities. Such technological advancements include the Lumi-Phos PRO chemiluminescent substrate, a new luminometer, and improved low-volume pipetting capabilities. These enhancements afford opportunities to develop immunoassays using reduced sample and reagent volumes (Figures 1 & 2), conserving precious patient samples, minimizing the carbon footprint of plastic packaging, and increasing the number of tests per reagent pack. Studies are presented herein for the Access TSH (3rd IS), Access βhCG (5th IS), and Access Hybritech Total PSA assays to evaluate analytical performance when using decreased sample/reagent volumes on the DxI 9000 analyzer (Figure 2).

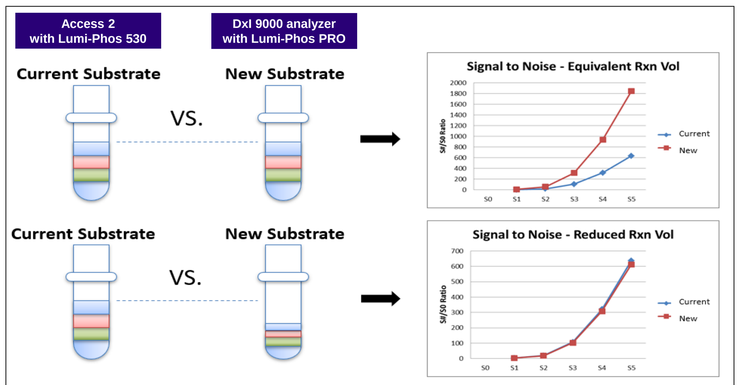

Figure 1. Graphical representation of reaction volumes and signal generation on the DxI 9000 analyzer with Lumi-Phos PRO (new substrate) compared to the Access 2 with Lumi-Phos 530 (current substrate). The DxI 9000 analyzer substrate produces greater signal compared to the Access 2 substrate with equivalent reaction volumes. Lumi-Phos PRO's increased signal production enables reduction of sample and reagent volumes required to maintain signal production while retaining sensitivity.

Assay	TSH 3rd IS		βhCG 5th IS		Total PSA	
Platform	Access 2	DxI 9000	Access 2	DxI 9000	Access 2	DxI 9000†
Sample Volume	50 µL	25 µL	25 µL	13 µL	25 µL	13 µL
Detection Reagent Volume	50 µL	25 µL	50 µL	25 µL	50 µL	25 µL
Capture Reagent Volume	25 µL	13 µL	50 µL	25 µL	50 µL	25 µL
Ancillary Reagent Volume	50 µL	25 µL	50 µL	25 µL	N/A	N/A

Figure 2. Comparison of volumes used in assay reactions on Access 2 and DxI 9000 analyzers. For Access TSH (3rd IS), Access βhCG (5th IS), and Access Hybritech Total PSA assays, volume requirements on the DxI 9000 analyzer are reduced by half.

METHODS

To assess performance when using proportionally reduced sample/reagent volumes on the DxI 9000 analyzer compared to standard sample/reagent volumes on the Access 2 Immunoassay System, within-laboratory precision was evaluated following CLSI EP05-A3,[1] limit of quantitation (LoQ) was estimated following CLSI EP17-A2,[2] and accuracy was assessed following CLSI EP09c, 3rd ed.[3]

Studies used multiple reagent pack lots, one or more calibrator lots, and multiple DxI 9000 analyzers and Access 2 instruments. Assay-specific quality controls were run in replicates of two for each assay on each day to verify the systems were in control. For the Access Hybritech Total PSA, results are presented using the Hybritech calibration values.

RESULTS

Results of sensitivity studies are summarized in the Figure 4 below for assays using reduced sample/reagent volumes on the DxI 9000 analyzer compared to standard volumes on the Access 2 system. Maximum observed limit of quantitation (LoQ) improved 1.4- to 3-fold on the DxI 9000 analyzer (Figure 4), despite employing ~50% reduction of sample/reagents (Figure 2). Precision (Figure 5) and accuracy studies (Figure 3) also showed acceptable performance.

METHODS COMPARISON

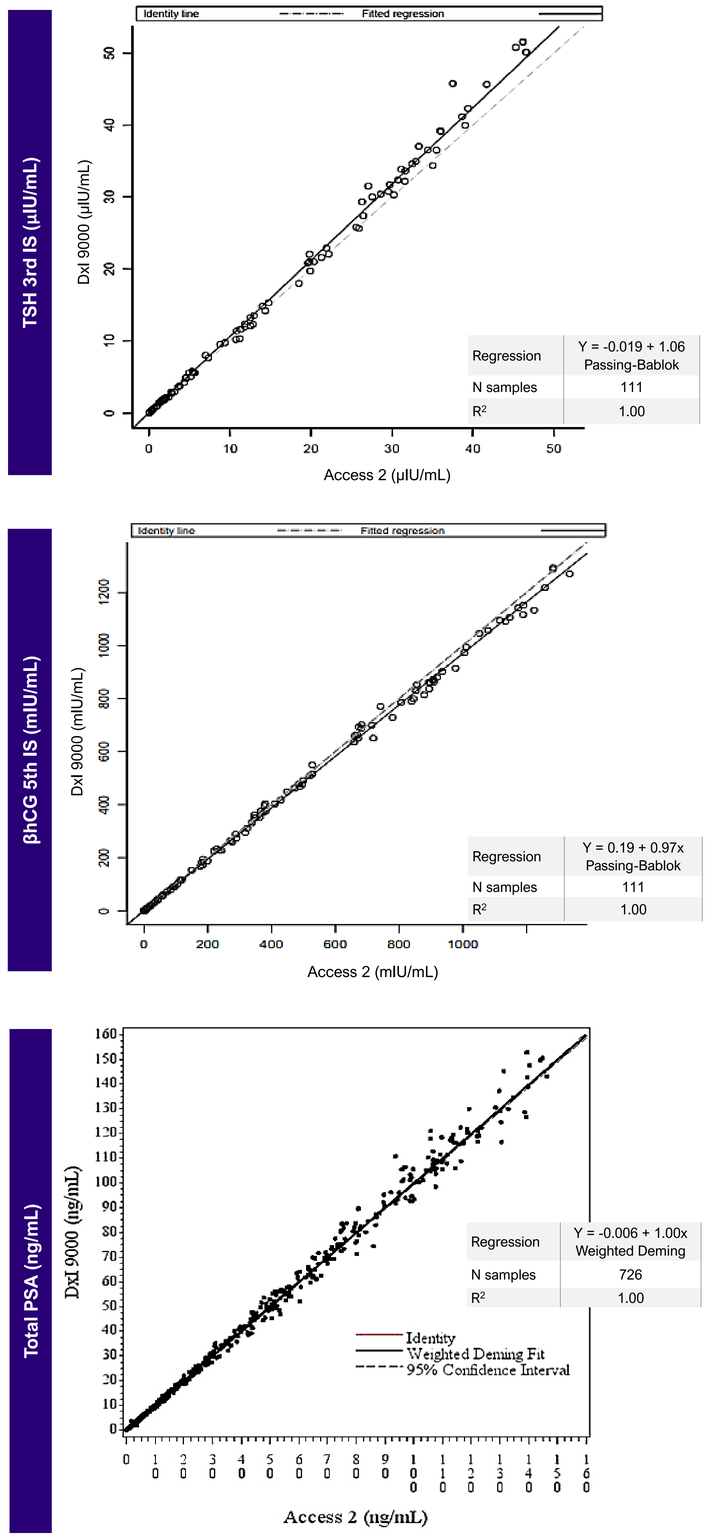

Figure 3. Methods comparison regression graphs and statistical descriptives for the Access TSH (3rd IS) (top), Access βhCG (5th IS) (middle), and Access Hybritech PSA (bottom) assays on the DxI 9000 analyzer (y-axis) vs the Access 2 (x-axis) predicate analyzer. All studies met their acceptance criteria.

LIMIT OF QUANTITATION

Assay	TSH 3rd IS		βhCG 5th IS		Total PSA	
Platform	Access 2	DxI 9000	Access 2	DxI 9000	Access 2	DxI 9000†
Maximum Observed 20% CV LoQ	0.003 µIU/mL	0.001 µIU/mL*	0.28 mIU/mL	0.2 mIU/mL	0.016 ng/mL	0.008 ng/mL

** LoQ estimate following EP17-A2 falls below LoD.*

Figure 4. Summary table for observed limit of quantitation (LoQ) results for Access 2 and DxI 9000 analyzers. All studies met acceptance criteria.

IMPRECISION

Assay	TSH 3rd IS		βhCG 5th IS		Total PSA	
Platform	Access 2	DxI 9000	Access 2	DxI 9000	Access 2	DxI 9000†
Within-Laboratory (Total) Imprecision CV%	2 – 7%	2.5 - 4.5%	2.4 – 8.9%	2.5 – 4.7%	4.2 – 5.2%*	2.2 – 4.9%

** UniCel DxI 800 data from Total PSA Instructions For Use*

Figure 5. Summary table for ranges of within-laboratory (total) imprecision values for Access 2 and DxI 9000 analyzers as measured across multiple samples. All studies met acceptance criteria.

CONCLUSIONS

The data herein present evidence for maintaining analytical performance goals when reducing sample and reagent volumes of assays on the DxI 9000 analyzer. The capabilities of the DxI 9000 analyzer, including its increased sensitivity, can be utilized to reduce the volume of sample and reagents, conserving patient sample and reducing packaging per test. The pipetting accuracy, paired with the detection capability of the DxI 9000 analyzer provide immunoassay developers opportunity to drive both improved low-end performance and conservation of resources.

References

1. CLSI. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition.* CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
2. CLSI. *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition.* CLSI document EP17-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
3. CLSI. *Measurement Procedure Comparison and Bias Estimation Using Patient Samples - Third Edition.* CLSI document EP09c, 3rd Ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.

* *The official name is DxI 9000 Access Immunoassay Analyzer.*
†The Access Hybritech PSA assay on the DxI 9000 Access Immunoassay Analyzer is pending clearance by the United States Food and Drug Administration; not yet available for in vitro diagnostic use in the US.