# ANALYTICAL PERFORMANCE CHARACTERISTICS OF THE NEW BECKMAN COULTER ACCESS PCT IMMUNOASSAY

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## BACKGROUND

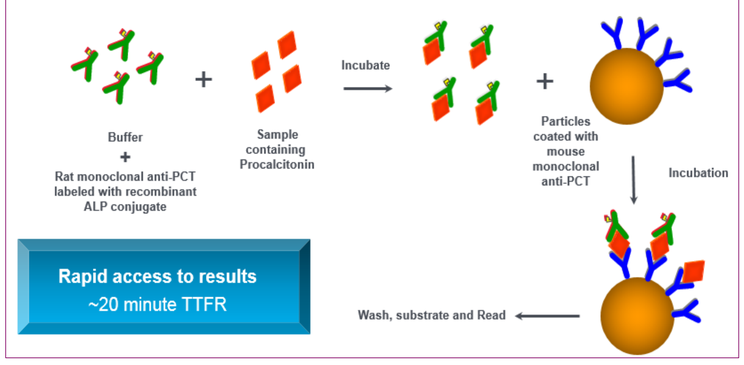
**Beckman Coulter recently developed and achieved CE Mark for a highly sensitive procalcitonin (PCT) immunoassay for use on the Access Immunoassay Systems†. PCT is a peptide of 116 amino acids with a molecular weight of ~13 kDa. PCT is produced in thyroid C-cells where it is converted to calcitonin in healthy individuals with less than 0.1 ng/mL PCT normally in circulation. PCT is a useful biomarker for diagnosis of sepsis and systemic inflammation because PCT levels increase in response to bacterial endotoxins and inflammatory cytokines.**

## METHODS

**The Access PCT assay is a sequential two-step sandwich assay. Monoclonal anti-PCT antibody alkaline phosphatase conjugate is added with sample to a reaction vessel and incubated. Paramagnetic particles* coated with a different monoclonal anti-PCT antibody are then added and incubated. After washing, a chemiluminescent substrate is added and light is generated which is directly proportional to the PCT concentration in the sample. The assay time to first result is ~20 minutes.**

***The Access PCT assay does not utilize biotin-streptavidin particle chemistry; as a result, it is not susceptible to biotin interference.**

ACCESS PCT: SEQUENTIAL TWO-STEP 'SANDWICH' ASSAY




## RESULTS

| Assay Characteristic | Access PCT Assay |
|---|---|
| Analytical Measuring Range | ~ 0.01 to 100 ng/mL<br>Up to 1000 ng/mL with automated dilution |
| Sample Volume | 35 µL |
| Tests per Pack | 50 |
| Calibrators S0-S6 | Lyophilized<br><u>Reconstituted Stability:</u><br>4 Hours at 20 to 25˚C<br>90 Days at -30 to -15˚C<br>3 freeze/thaws |
| Open-Pack/Stored Curve Stability | 42 Days |
| Sample Types | Serum (gel or no gel)<br>Lithium Heparin Plasma<br>EDTA Plasma |
| Hook Effect | No hook effect up to 5,000 ng/mL |

| | | Within-Run (Repeatability) | | Between-Run | | Between-Day | | Within Lab (Total Imprecision) | |
|---|---|---|---|---|---|---|---|---|---|
| Sample | Grand Mean (ng/mL) (n=80) | SD (ng/mL) | CV (%) | SD (ng/mL) | CV (%) | SD (ng/mL) | CV (%) | SD (ng/mL) | CV (%) |
| QC 1 | **0.68** | 0.013 | 1.9 | 0.014 | 2.1 | 0.015 | 2.2 | 0.024 | **3.6** |
| QC 2 | **2.15** | 0.040 | 1.9 | 0.056 | 2.6 | 0* | N/A | 0.069 | **3.2** |
| QC 3 | **20.65** | 0.333 | 1.6 | 0.531 | 2.6 | 0.228 | 1.1 | 0.667 | **3.2** |
| Sample 1 | **0.090** | 0.003 | 3.2 | 0.002 | 2.7 | 0.005 | 5.8 | 0.006 | **7.2** |
| Sample 2 | **0.18** | 0.006 | 3.2 | 0.003 | 1.7 | 0.008 | 4.3 | 0.010 | **5.6** |
| Sample 3 | **0.27** | 0.008 | 2.8 | 0.003 | 1.0 | 0.009 | 3.2 | 0.012 | **4.4** |
| Sample 4 | **0.43** | 0.011 | 2.6 | 0.014 | 3.3 | 0.016 | 3.8 | 0.024 | **5.7** |
| Sample 5 | **1.41** | 0.039 | 2.8 | 0.034 | 2.4 | 0.048 | 3.4 | 0.070 | **5.0** |
| Sample 6 | **7.59** | 0.175 | 2.3 | 0.121 | 1.6 | 0.239 | 3.2 | 0.320 | **4.2** |
| Sample 7 | **76.31** | 1.753 | 2.3 | 1.773 | 2.3 | 1.452 | 1.9 | 2.885 | **3.8** |

*Default value when estimated variance was negative

**Figure 1** A precision study was performed according to CLSI EP05-A3[1] using serum samples run over 20 days. The total imprecision for serum sample mean PCT concentrations from 0.090 to 76.31 ng/mL resulted in %CV values of 3.8 to 7.2.

| | | Within-Run | | Between-Run | | Between-Day | | Between Site | | Between Lot | | Reproducibility | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sample | Grand Mean (ng/mL) (n=176) | SD (ng/mL) | CV (%) | SD (ng/mL) | CV (%) | SD (ng/mL) | CV (%) | SD (ng/mL) | CV (%) | SD (ng/mL) | CV (%) | SD (ng/mL) | CV (%) |
| QC 1 | **0.68** | 0.015 | 2.2 | 0.009 | 1.3 | 0.013 | 1.9 | 0.008 | 1.2 | 0.006 | 0.9 | 0.024 | **3.5** |
| QC 2 | **2.20** | 0.046 | 2.1 | 0.039 | 1.7 | 0* | N/A | 0.049 | 2.2 | 0.019 | 0.9 | 0.079 | **3.6** |
| QC 3 | **21.01** | 0.418 | 2.0 | 0.308 | 1.5 | 0.368 | 1.8 | 0.652 | 3.1 | 0* | N/A | 0.911 | **4.3** |
| Sample 1 | **0.090** | 0.003 | 3.2 | 0.002 | 2.6 | 0.003 | 2.9 | 0.001 | 1.6 | 0.002 | 2.2 | 0.005 | **5.7** |
| Sample 2 | **0.18** | 0.005 | 2.8 | 0.004 | 2.3 | 0.003 | 1.7 | 0.003 | 1.5 | 0.004 | 2.0 | 0.008 | **4.7** |
| Sample 3 | **0.27** | 0.008 | 2.8 | 0.005 | 1.8 | 0.006 | 2.1 | 0* | N/A | 0.004 | 1.4 | 0.011 | **4.2** |
| Sample 4 | **0.43** | 0.011 | 2.6 | 0.009 | 2.2 | 0.006 | 1.4 | 0.005 | 1.1 | 0.007 | 1.7 | 0.018 | **4.1** |
| Sample 5 | **1.41** | 0.039 | 2.8 | 0.026 | 1.8 | 0* | N/A | 0.028 | 2.0 | 0.024 | 1.7 | 0.060 | **4.2** |
| Sample 6 | **7.79** | 0.195 | 2.5 | 0.135 | 1.7 | 0.096 | 1.2 | 0.321 | 4.1 | 0.124 | 1.6 | 0.429 | **5.5** |
| Sample 7 | **77.03** | 2.218 | 2.9 | 1.157 | 1.5 | 0.284 | 0.4 | 1.529 | 2.0 | 1.412 | 1.8 | 3.266 | **4.2** |

*Default value when estimated variance was negative

**Figure 2** A reproducibility precision study was performed at three external sites using serum samples run in duplicate with two runs per day over five days. The reproducibility across sites for serum sample mean PCT concentrations from 0.090 to 77.03 ng/mL resulted in %CV values of 3.5 to 5.7.

| Parameter | Criteria (ng/mL) | Maximum Observed Result (ng/mL) |
|---|---|---|
| **LoB** | **≤0.005** | **0.001** |
| **LoD** | **≤0.01** | **0.002-0.003** |
| Serum | | **0.002** |
| Lithium Heparin Plasma | | **0.002** |
| EDTA Plasma | | **0.003** |
| **LoQ 20% CV** | **≤0.02** | **0.002-0.003** |
| Serum | | **0.002** |
| Lithium Heparin Plasma | | **0.002** |
| EDTA Plasma | | **0.003** |

**Figure 3** Studies performed based on CLSI EP17-A2[2], the Access PCT assay exhibited a Limit of Blank of 0.001 ng/mL, and a Limit of Detection (LoD) and Limit of Quantitation (LoQ) of 0.002 ng/mL in Serum and Lithium Heparin Plasma, and 0.003 ng/mL in EDTA Plasma.

| Sample Size | Median (ng/mL) | 95% Upper Reference Interval (ng/mL) |
|---|---|---|
| **202** | **0.025** | **0.065** |

**Figure 4** PCT reference interval testing was performed at one external site on an Access 2 immunoassay system using 202 serum samples from approximately equal numbers of apparently healthy male and female subjects ≥21 years of age.

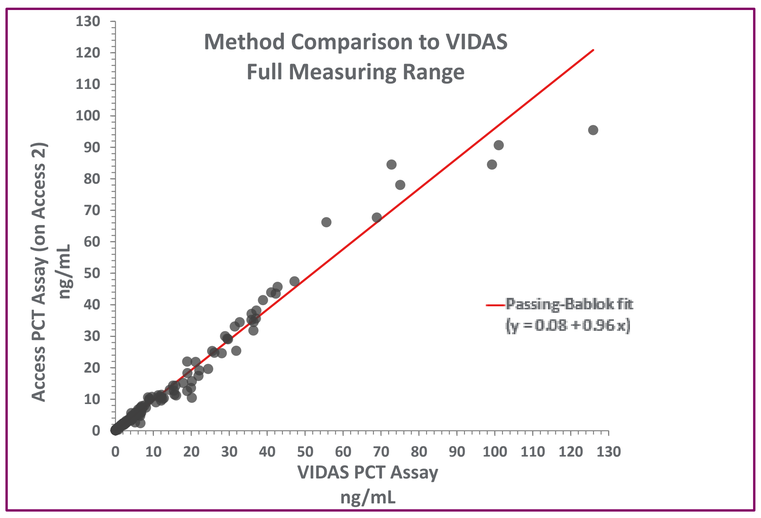



**Figure 5** Method Comparison with 229 patient samples using the Access PCT assay and the VIDAS® B·R·A·H·M·S PCT™ assay gave a Passing-Bablok Slope of 0.96 and Intercept of 0.08 ng/mL. The Pearson correlation coefficient was 0.99.

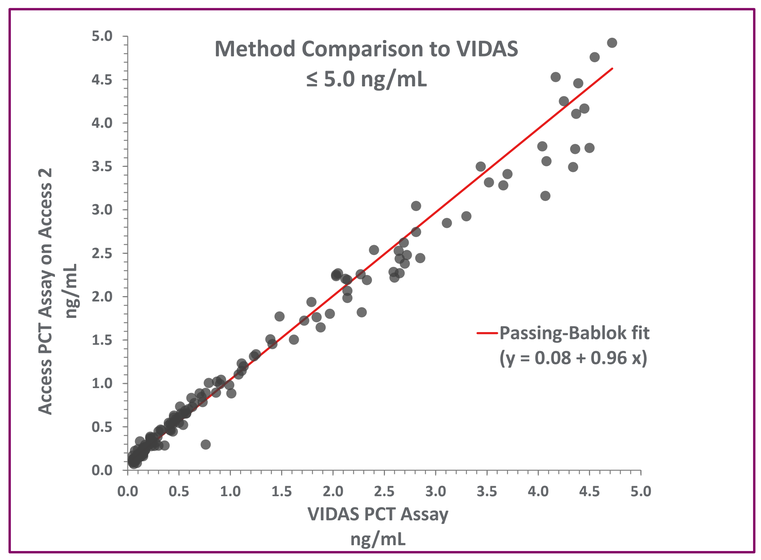



**Figure 6** Method Comparison with patient samples ≤ 5 ng/mL using the Access PCT assay and the VIDAS® B·R·A·H·M·S PCT™ assay gave a Passing-Bablok Slope of 0.96 and Intercept of 0.08 ng/mL. The Pearson correlation coefficient was 0.99.

| | VIDAS PCT | | |
|---|---|---|---|
| Access 2 PCT | ≤ 0.5 ng/mL | > 0.5 ng/mL | Total |
| ≤ 0.5 ng/mL | 85 | 1 | 86 |
| > 0.5 ng/mL | 10 | 164 | 174 |
| Total | 95 | 165 | 260 |
| **Overall agreement = 95.8%** | | | |

| | VIDAS PCT | | |
|---|---|---|---|
| Access 2 PCT | ≤ 2 ng/mL | > 2 ng/mL | Total |
| ≤ 2 ng/mL | 133 | 2 | 135 |
| > 2 ng/mL | 0 | 125 | 125 |
| Total | 133 | 127 | 260 |
| **Overall agreement = 99.2%** | | | |

**Figure 7** The analytical concordance between the Access PCT assay and the VIDAS® B·R·A·H·M·S PCT™ assay at the PCT levels of 0.5 and 2.0 ng/mL were 95.8% and 99.2%, respectively.

## CONCLUSIONS

**The Access PCT assay is a highly sensitive and precise assay, demonstrating strong correlation and concordance to a well-established predicate PCT method at clinically relevant levels.**

## REFERENCES

1. CLSI EP05-A3:2014 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition.
2. CLSI EP17-A2:2012 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, Second Edition.

†Pending submission and clearance by the United States Food and Drug Administration and Health Canada; not yet available for in vitro diagnostic use in the US or Canada.



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