# Novel Use of POCT Devices for Diagnosis of Bacterial Infections and Sepsis in Critical Care Environments

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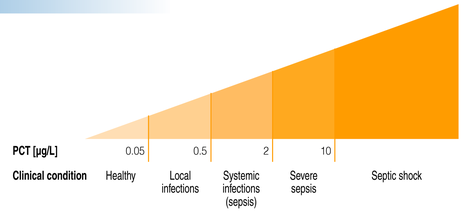
## Introduction



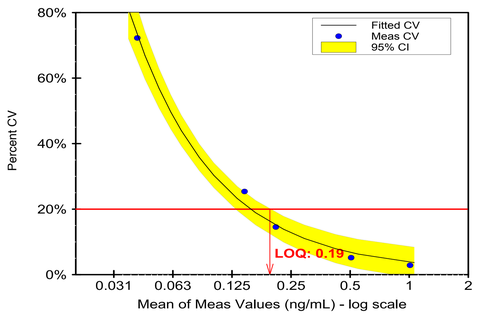

Procalcitonin (PCT) is one of the most effective and specific biomarkers used for diagnosis of bacterial infections and risk assessments for sepsis and septic shock. Based on the blood levels of PCT, clinicians are able to differentiate viral infections from systemic bacterial infections, and are able to tell if a patient is at high risk of sepsis, severe sepsis, or sepsis shock in critical care environment. PCT values can also assist doctors in making therapeutic decisions on initiation and duration of antibiotics. For example, PCT levels of < 0.25 ng/mL are more indicative of viral but not systemic bacterial infections, whereas PCT levels of > 0.5 ng/mL are more indicative of systemic bacterial infections; and levels of >10.0 ng/mL are strong indication of septic shock1. Due to the rapid progression of disease state typically found in patients with sepsis in critical care environments such as the intensive care units or emergency rooms in hospitals, it is not always practical to send samples out to the lab for testing. The delay from transporting patient samples to labs, waiting on technicians to evaluate the sample, and the return of the diagnosis to the attending medical personnel can limit the available options as to how to effectively treat the patient. By implementing point of care testing (POCT) devices within the patient's near vicinity, medical personnel will be able to rapidly and efficiently diagnose a patient allowing proper treatment before the disease state is able to progress.

1. Harbeth S, et al., Diagnostic value of procalcitonin, interleukin-6, and interleukin-8 in critically ill patients admitted with suspected sepsis. Am J Respir Crit Care Med 2001; 164:396-402

## Results

The assay linearity ranges from 0.19 to 12.00 ng/mL. Using CLSI guidelines, the limits of blank, detection, and quantitation were 0.09, 0.14, and 0.19 ng/mL. Intra and total precision were determined using the CLSI Evaluated Protocol for Precision. Three samples containing 0.60, 1.00, and 8.00 ng/mL PCT tested two times a day in duplicates over the course of ten working days. The intra-assay precision (CV) for the three samples was < 8.0% and the total CV was < 7.4%. A comparison of assay values obtained from serum samples using the Diazyme PCT POC Test Kit and a currently marketed chemiluminescent assay gave the following linear regression data: slope = 0.9906 (95% confidence interval of 0.973 to 1.035), an intercept of 0.038 (95% confidence interval of -0.032 to 0.221), and a correlation coefficient (R2) of 0.9957 (95% confidence interval of 0.9917 to 0.9977).

### Graph 1 - Precision Profile

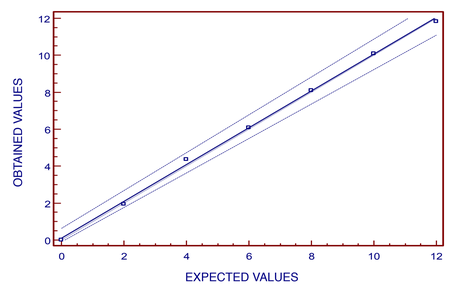



Evaluation of the Limit of Quantitation using five serially diluted samples with a CV cutoff at 20%

### Table 1 - Limit of Quantitation

| | | 1.00 ng/mL | 0.50 ng/mL | 0.25 ng/mL | 0.13 ng/mL | 0.07 ng/mL |
|---|---|---|---|---|---|---|
| Day 1 | 1 | 1.03 | 0.52 | 0.20 | 0.14 | 0.05 |
| | 2 | 0.98 | 0.45 | 0.21 | 0.08 | 0.00 |
| | 3 | 1.01 | 0.52 | 0.26 | 0.22 | 0.00 |
| | 4 | 0.95 | 0.47 | 0.17 | 0.17 | 0.02 |
| | 5 | 1.02 | 0.51 | 0.16 | 0.12 | 0.06 |
| Day 2 | 1 | 0.99 | 0.48 | 0.20 | 0.15 | 0.07 |
| | 2 | 0.97 | 0.51 | 0.24 | 0.07 | 0.06 |
| | 3 | 1.03 | 0.50 | 0.22 | 0.14 | 0.03 |
| | 4 | 1.00 | 0.51 | 0.23 | 0.14 | 0.02 |
| | 5 | 1.02 | 0.47 | 0.20 | 0.12 | 0.00 |
| Day 3 | 1 | 1.04 | 0.52 | 0.16 | 0.15 | 0.06 |
| | 2 | 1.05 | 0.50 | 0.22 | 0.22 | 0.04 |
| | 3 | 1.03 | 0.56 | 0.25 | 0.17 | 0.04 |
| | 4 | 0.98 | 0.52 | 0.23 | 0.12 | 0.03 |
| | 5 | 0.96 | 0.49 | 0.15 | 0.14 | 0.06 |
| Day 4 | 1 | 1.04 | 0.51 | 0.22 | 0.11 | 0.07 |
| | 2 | 1.02 | 0.49 | 0.21 | 0.16 | 0.04 |
| | 3 | 1.03 | 0.53 | 0.20 | 0.14 | 0.11 |
| | 4 | 1.04 | 0.51 | 0.19 | 0.12 | 0.09 |
| | 5 | 1.04 | 0.54 | 0.21 | 0.13 | 0.07 |
| Day 5 | 1 | 1.03 | 0.53 | 0.26 | 0.18 | 0.00 |
| | 2 | 0.97 | 0.52 | 0.22 | 0.14 | 0.05 |
| | 3 | 1.02 | 0.48 | 0.21 | 0.21 | 0.02 |
| | 4 | 0.99 | 0.47 | 0.24 | 0.15 | 0.00 |
| | 5 | 1.00 | 0.54 | 0.17 | 0.13 | 0.04 |
| Mean | | 1.01 | 0.51 | 0.21 | 0.14 | 0.04 |
| SD | | 0.03 | 0.03 | 0.03 | 0.04 | 0.03 |
| CV | | 2.8% | 5.1% | 14.2% | 24.9% | 70.8% |

### Graph 2 - Linearity




Evalutation of linearity using a 7 level serially diluted sample set from 12.0 ng/mL to 0.0 ng/mL

### Table 2 - Linearity

| | Expected | Obtained | Bias |
|---|---|---|---|
| Level 7 | 12 | 11.82 | 1.5% |
| Level 6 | 10 | 10.09 | -0.9% |
| Level 5 | 8 | 8.1 | -1.3% |
| Level 4 | 6 | 6.08 | -1.3% |
| Level 3 | 4 | 4.36 | -9.1% |
| Level 2 | 2 | 1.95 | 2.7% |
| Level 1 | 0 | 0 | N/A |

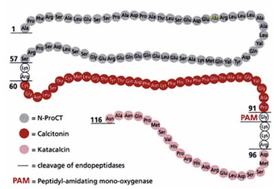
## Method

The Diazyme PCT POC Test Kit utilizes a single use test cartridge containing 2 separate reagents which is inserted into the SMART Point of Care Device. The assay is a latex enhanced immunoturbidimetric format measuring concentration of the analyte via agglutination of latex particles. Sample is loaded into the test cartridge and is inserted in to the device. The test is completely automated utilizing parameters programmed via an RFID calibration card. Reagent addition, mixing and incubation time is all automated in less than 10 minutes and upon completion, the cartridge is ejected and the determined PCT concentration is displayed.

## Conclusion

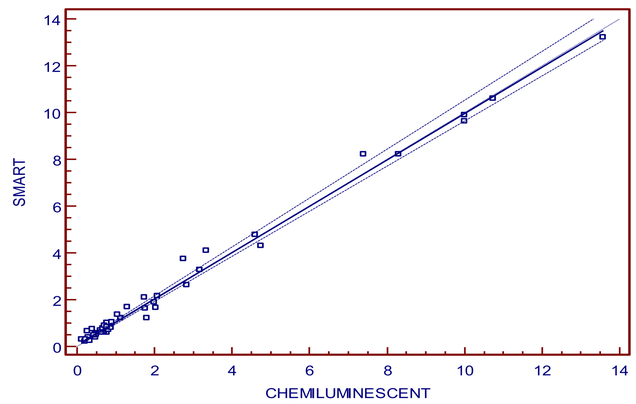
The Diazyme PCT POC Test Kit provides accurate and rapid results for the determination of PCT concentrations in critical care patients susceptible to systemic infections comparable to currently marketed devices.

By adapting procalcitonin assays to a faster, smaller, simpler format, caregivers can properly diagnose patients for systemic infection without the fear of the condition progressing to septic shock. The use of POCT platform in intensive care units, emergency rooms, and other facilities for critical care will provide rapid analysis of patient's condition, expedite the treatment process, and reduce the patient mortality due to sepsis and septic shock.




Molecular Structure of Procalcitonin

### Graph 3 - Method Comparison




Comparison of patient sample values (ng/mL) using Diazyme SMART PCT Assay and marketed Chemiluminscent PCT Assay

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