Novel POC Devices for Testing Procalcitonin (PCT) in ER and ICU Settings

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Background: Procalcitonin (PCT) is a 116 amino acid prohormone formed by the endopeptidase-cleaved preprocalcitonin in response to stimulation by bacterial products and cytokines. PCT is uniformly expressed in human body in response to systemic sepsis which make it one of the most effective and specific biomarkers for diagnosis of bacterial infections, sepsis, and septic shock. In healthy subjects, the PCT levels in circulation are very low. PCT levels of >0.50 ng/mL generally indicate a systemic bacterial infection, and levels of >10.0 ng/mL are a strong indicator of septic shock. Due to the rapid progress of disease state typically found in patients with sepsis, sending samples out for testing is not conducive for urgent care and can limit treatment options. Studies show patients have an 80% increased rate of survival when treated within the first hour of displayed symptoms. To address this need PCT point of care test (POCT) was developed for use on a small device (Cube or Smart) that can be utilized in ER or ICU settings. The results can be obtained in less than 10 minutes.

Methods: Diazyme Cube or Smart PCT POCT Kit is based on latex enhanced immunoturbidimetric method for use on Diazyme's Cube or Smart analyzer. When an antigen-antibody reaction occurs between PCT in a sample and anti-PCT antibody, which has been sensitized to latex particles, agglutination results. The degree of the turbidity caused by agglutination can be measured optically at 700 nm and is proportional to the amount of PCT in the sample. The instrument calculates the PCT concentration of patient specimen by use of a lot specific calibration curve that is stored in an RFID card provided with each Cube or Smart PCT POC kit. The RFID card contains the lot number and lot specific calibration curve and is required for every sample tested.

Results:

Precision: The precision of Diazyme Cube and Smart PCT POCT Kit was evaluated according to CLSI EP5-A2 guideline. Six samples containing 0.27 0.61, 1.30, 2.40, 5.48, and 9.12 ng/mL PCT were tested over 10 days, 2 runs a day in 2 replicates on Cube analyzer and total CV% were 12.4%, 9.2%, 8.8%, and 4.5% respectively; six samples containing 0.20 0.51, 1.09, 2.47, 5.45, and 8.26 ng/mL PCT were tested similarly on Smart analyzer and total CV% were 13.4%8.8%, 5.5%, 5.0%, and 4.4% respectively.

Sensitivity: The LOB, LOD, and LOQ of the Diazyme Cube and Smart PCT POCT Kit were determined according to CLSI EP17-A2. The LOB, LOD, and LOQ were determined to be 0.04 ng/mL, 0.11 ng/mL, and 0.21 ng/mL for Cube and 0.075, 0.16, and 0.21 ng/mL for Smart.

Linearity: The eleven level linearity set was prepared by mixing a pooled PCT spiked plasma sample containing 10.52 ng/mL PCT and PCT depleted matrix at different proportions according to CLSI EP6-A. The linear regression results are as follows: R^2=0.999, slope=1.01for CUBE and R^2=0.992, slope=0.990 for Smart. The Diazyme Cube or Smart PCT POCT Kit is linear up to 10 ng/mL PCT.

Method Comparison: Following CLSI EP9-A2, 40 plus serum samples were tested with the Diazyme Cube and Smart PCT POCT Kit and the obtained results were compared with a commercial Kit. The linear regression results are as follows: R^2 = 0.9811, slope =0.990, intercept = 0.031 for Cube and R^2 = 0.9919, slope = 0.990, y-intercept = 0.051for Smart.

Conclusion: The Diazyme Cube and Smart PCT POCT Kit is an effective and accurate device for diagnosing sepsis. It supports early diagnosis for critically ill patients and allows for better clinical decision making by providing additional information in under 10 minutes.