A-216

510(k) clearance of the universally applicable DiaSys Procalcitonin FS test for the diagnosis of sepsis

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To obtain U.S. market authorization (510(k)) for the Procalcitonin FS assay developed by DiaSys Diagnostic Systems GmbH, an additional set of data had to be generated. This included studies on HAMA and total protein interference, sample stability, and medical concordance. The inclusion of these new data demonstrates the robustness of the PCT FS assay and confirms its suitability in routine clinical use.

PURPOSE

Sepsis is a major global health concern, associated with high incidence and mortality rates. Procalcitonin (PCT) is widely recognized as the best commercially available biomarker for the diagnosis of sepsis. In 2020, DiaSys has launched an immunoturbidimetric assay for the quantitative determination of PCT in human serum and plasma in Europe under CE marking. To support U.S. market authorization, the U.S. Food and Drug Administration (FDA) requested additional technical data as part of the 510(k) submission. These included evaluations of human anti-mouse antibody (HAMA) interference, total protein interference, sample stability, Cohen's kappa at clinically relevant cut-off values, and negative and positive percent agreement with a predicate device.

MATERIALS & METHODS

All evaluations were performed in human serum and plasma using the Abbott ARCHITECT c8000 as selected analyzer. An acceptable recovery range of ±15% was predefined. HAMA interference was assessed at concentrations up to 480 ng/mL by spiking highly concentrated HAMA material into a human sample containing approximately 0.5 ng/mL PCT. Total protein interference was evaluated at concentrations up to 139 g/L by spiking bovine serum albumin (BSA) into a human sample containing approximately 0.5 ng/mL PCT.

For sample stability testing, fifteen human serum and plasma samples were spiked with PCT concentrations covering the full analytical measurement range. Aliquots were stored for 24 hours at 20–25°C, 5 days at 2–8°C, and 14 days at −20°C. Stability was assessed using linear regression analysis and scatter plots.

Method comparison was conducted using 210 human samples analyzed with the PCT FS assay and the bioMérieux VIDAS® Procalcitonin reference method. Negative percent agreement (NPA) and positive percent agreement (PPA) were calculated using 2×2 contingency tables at clinical cut-off values of 0.5 and 2.0 ng/mL. Cohen's kappa was calculated using MedCalc® Statistical Software (version 23.1.7). Acceptance criteria for NPA and PPA were ±10%.

RESULTS & DISCUSSION

The immunoturbidimetric PCT FS assay showed no evidence of interference by HAMA in either serum and plasma matrix at the clinically relevant decision thresholds of 0.5 ng/mL (Figure 1) and 2.0 ng/mL. This finding was expected given the use of goat-derived polyclonal antibodies in the assay design. Similarly, total protein concentrations of up to 139 g/L had no effect on assay recovery in either matrix at both clinically relevant cut-off values. These interference studies demonstrate that the DiaSys PCT FS assay is robust and reliable, even under extreme physiological conditions.

Human serum and plasma samples remained stable under all tested storage temperatures and durations (Figure 2). Recovery for every individual sample remained within ±10% of the initial value. Furthermore, least-squares regression analysis against the concentration measured at baseline (time 0) yielded coefficients of determination (R2) of at least 0.9988 and regression slopes of at least 0.9456 across all tested conditions. These results demonstrate that storage under the evaluated conditions does not affect the performance of the PCT FS assay. This stability may be attributed to the use of polyclonal antibodies, which recognize a broader range of antigenic epitopes.

Finally, the ability of the PCT FS test to support correct clinical decision-making was assessed by determining Cohen's kappa relative to the predicate device. At the 0.5 ng/mL cut-off, the assay achieved a Cohen's kappa of 0.981 (95% CI: 0.954–1.000), with a negative percent agreement (NPA) of 98.0% (95% CI: 92.9%–99.8%) and a positive percent agreement (PPA) of 100% (95% CI: 96.7%–100.0%) (Table 1). At the 2.0 ng/mL cut-off Cohen's kappa was determined with 0.955 (95% CI: 0.912–0.999), with a negative percent agreement (NPA) of 100.0% (95% CI: 97.5%–100.0%) and a positive percent agreement (PPA) of 94.0% (95% CI: 85.4%–98.4%).

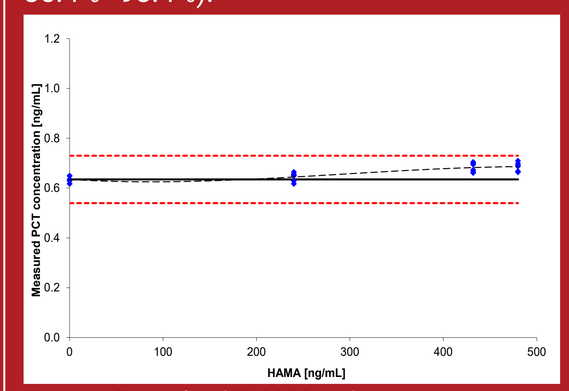

Figure 1. Example of HAMA interference measurement in plasma at cut-off 0.5 ng/mL PCT.

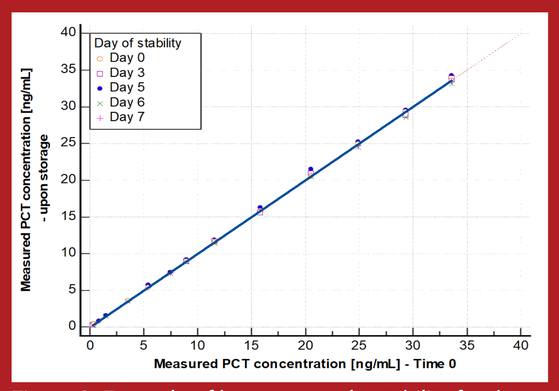

Figure 2. Example of human sample stability for the storage at 2-8°C in serum up to 7 days.

	Predicate device		
DiaSys PCT FS	PCT < 0.5 ng/mL	PCT ≥ 0.5 ng/mL	
PCT < 0.5 ng/mL	97	0	97 (46.2%)
PCT ≥ 0.5 ng/mL	2	111	113 (53.8%)
	99 (47.1%)	111 (52.9%)	210
Cohen's Kappa (95% CI) = 0.981 (0.954 to 1.000)			

Table 1. Analysis of the medical concordance at the cut-off 0.5 ng/mL (Cohen's kappa).

CONCLUSION

The PCT FS assay received FDA 510(k) clearance on May 9, 2025 (K242294), enabling its use as an aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock.