

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

K082631

B. Purpose for Submission:

Clearance of new assay

C. Measurand:

Protein S

D. Type of Test:

Clotting

E. Applicant:

R2 Diagnostics

F. Proprietary and Established Names:

ThromboTek PSe

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7290

2. Classification:

II

3. Product code:

GGP

4. Panel:

81 Hematology

H. Intended Use:

1. Intended use(s):

The ThromboTek PSe is a quantitative assay for the determination of protein S activity in human plasma by clotting.

2. Indication(s) for use:

Deficiencies of protein S are associated with an increased risk of thrombosis.

3. Special conditions for use statement(s):

4. Special instrument requirements:

I. Device Description:

ThromboTek PSe is a tissue factor pathway based clotting assay. The assay activator is a lyophilized preparation incorporating rabbit thromboplastin, calcium, buffer, and stabilizers. The remaining components of the assay are lyophilized activated Protein C, lyophilized human plasma depleted of Protein S, imidazole buffered saline, and deionized water containing a preservative for reconstitution of the lyophilized components.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Diagnostica Stago StaClot® Protein S

2. Predicate 510(k) number(s):

K913424

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative determination of	Same

Similarities		
Item	Device	Predicate
	functional Protein S activity	
Sample requirement	Citrated plasma	same
Assay principle	Clotting	same
Reagents	Activator, aPC, Protein S deficient plasma	same

Differences		
Item	Device	Predicate
Linearity	1- 156%	10 -105%
Sensitivity	1%	8%
Reagents	Buffered saline and reconstitution solution included in assay kit	Owen-Koller buffer and calcium chloride purchased separately, reconstitution grade water provided by user

K. Standard/Guidance Document Referenced (if applicable):

CLSI/NCCLS EP5-A2, “Evaluation of Precision Performance of Quantitative Measurement Methods Approved Guideline- Second Edition”

CLSI/NCCLS EP15-A2, “User Verification of Performance for Precision and Trueness: Approved Guideline-Second Edition”, 2005

H21-A5, “Collection, Transport and Processing of Blood Samples for Testing Plasma-based Coagulation Assays and Molecular Hemostasis Assays; Approved Guideline-Fifth Edition”, 2008

L. Test Principle:

The Tissue Factor pathway of coagulation is activated when endogenous FVII or activated FVIIa in the sample plasma is mixed with tissue factor in the presence of calcium. This TF/FVIIa complex activates Factor X (FX) to FXa. Factor Xa complexes with activated Factor V (FVa) on a lipid surface in the presence of calcium to form a prothrombinase complex. The prothrombinase complex activates prothrombin to thrombin. Thrombin cleaves fibrinogen to fibrin leading to formation of a solid clot.

Activated Protein C (aPC) in the presence of its cofactor Protein S degrades FVa, reducing the efficiency of the prothrombinase complex. When there is an excess of aPC, the concentration of Protein S in the patient sample is rate limiting. Thus, the

time for the patient plasma to clot is proportional to the concentration of the PS in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were conducted in accordance with CLSI/NCCLS Guideline EP5-A2, *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition*. Three lots of the assay kit was used to determine precision in a two run per day, twenty day exercise on an AMAX 200 analyzer in mechanical mode using a normal and abnormal plasma.

Plasma	Repeatability	Total
Normal	4.9%	5.7%
Abnormal	7.8%	9.2%

b. *Linearity/assay reportable range:*

Three lots of linearity testing using ISTH/SCC plasma demonstrated ThromboTek PSe linearity of 10- 156% Protein S.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Assay recommends the use of pooled normal plasma or purchased reference plasma for calibration, and the use of purchased quality control material for QC

d. *Detection limit:*

Lower limit of detection was determined by testing 30 replicates of the assay buffer on 3 lots of the ThromboTek PSe assay. The mean, standard deviation (SD), and mean + 3SD of the clot times were calculated for all three lots. The LoD was calculated as 1%.

e. *Analytical specificity:*

Hemoglobin, bilirubin, lipid, and heparin interference was tested by spiking the interferent into pooled normal plasma and preparing serial dilutions. The maximum concentration tolerated in the assay was defined as the highest concentration of interferent resulting in a <10% difference in the base result. The maximum concentrations were:

Interferent	Added Interferent	Maximum concentration Tested	Maximum tolerated concentration
Hemolysis	Hemoglobin	500 mg/dL	500 mg/dL
Icterus	Unconjugated Bilirubin	20 mg/dL	20 mg/dL
Lipemia	IntraLipid®	2,000 mg triglycerides/dL	2,000 mg triglycerides/dL
Heparin	Heparin	2.0 Units/mL	1.0 units/mL

f. *Assay cut-off:*

n/a

2. Comparison studies:

a. *Method comparison with predicate device:*

174 patient samples were assayed on multiple lots of ThromboTek PSe. Data was collected at two sites, one using an Trinity Biotech AMAX 200 analyzer and the other a Diagnostica Stago STA4, and yielded correlation statistics of $y = 1.711x - 8.89$, $r = 0.895$

b. *Matrix comparison:*

n/a

3. Clinical studies:

a. *Clinical Sensitivity:*

n/a

b. *Clinical specificity:*

n/a

c. Other clinical supportive data (when a. and b. are not applicable):

n/a

4. Clinical cut-off:

n/a

5. Expected values/Reference range:

120 normal donors (85 females, 35 males) were assayed on 3 kits of the ThromboTek PSe. Mean, and two standard deviation ranges were calculated for males (62 – 209), females (45 – 183), and combined male and female (47-193)

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.