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

A. 510(k) Number:

K043571

B. Purpose for Submission:

Clearance of a new assay

C. Measurand:

Functional Protein S

D. Type of Test:

Clotting Assay

E. Applicant:

Precision BioLogic Inc.

F. Proprietary and Established Names:

CRYOcheck™ Clot S™

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.7290

2. Classification:

   Class II

3. Product code:

   GGP

4. Panel:

   81

H. Intended Use:

1. Intended use(s):

   Cryo*CHECK*™ Clot S™ is a clot based assay intended for the quantitative determination of protein S activity in citrated human plasma.

2. Indication(s) for use:

   Cryo*CHECK*™ Clot S™ is used to diagnose protein S deficiency (congenital or acquired) which is indicative of an increased risk of thromboembolism. A deficiency in protein S may produce recurrent thrombotic episodes.

3. Special conditions for use statement(s):

4. Special instrument requirements:

I. Device Description:

The Cryo*CHECK*™ Clot S™ assay consists of Protein S Deficient Plasma which is derived from citrated pooled normal human plasma that has been depleted of protein S by immunoadsorption, and Clot S Activator, which contains activated protein C, Russell's viper venom, heparin neutralizing agents, buffers and stabilizers. The assay also requires Precision BioLogic Cot C & S Diluent which is available separately.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Diagnostica Stago STA®-Staclot® Protein S

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

   K913424

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative measurement of	same

Similarities		
Item	Device	Predicate
	functional Protein S	
Method	Clot based	same

Differences		
Item	Device	Predicate
Format	Frozen	Lyophilized

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

L. Test Principle:

The Cryo*CHECK*™ Clot S™ assay initiates the common pathway of the coagulation cascade through the Clot S Activator reagent. The Russell's viper venom (RVV-X) in the activator converts factor X to Xa in the presence of activated protein C (APC), bypassing all factors above the common pathway. When mixed with protein S deficient plasma, samples from patients with a protein S deficiency or dysfunction will have shortened Cryo*CHECK*™ Clot S™ clotting times relative to samples with normal levels of functional protein S. The clotting time is proportional to the amount of functional protein S in the patient's plasma which is quantified using a calibration curve.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Intra-assay precision was determined by testing one normal sample, and one sample closes to the clinically critical decision point 20 times each, and calculating %CV. Results – Normal 3.9%, Abnormal 8.2%.

   Inter-assay precision was determined by testing one normal sample and one abnormal sample over seven days. Seven different calibration curves and two different operators were used. On days 1-6 each sample was run 5X in sequence. On day 7 each sample was run 20X in sequence. Results –Normal 8.7%CV, Abnormal 11.2% CV.

   b. Linearity/assay reportable range:

   Aliquots of a normal plasma sample with a high protein S level was diluted in

protein S deficient plasma to produce a series of samples with known protein S values. The samples were tested with the Cryo*CHECK*™ Clot S™ assay in four replicates and the protein S values were determined. Results demonstrated linearity between 10-140%.

Samples greater that 140% are recommended to be diluted 1:20 and retested.

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

d. *Detection limit:*

e. *Analytical specificity:* A heparin interference study was performed using plasma with a known normal protein S activity. Baseline protein S was measured, and then aliquots of the plasma were then prepared to contain I creased levels of unfractionated heparin (UFH) or low molecular weight heparin (LMWH). Results indicated that Cryo*CHECK*™ Clot S™ is unaffected by UFH and LMWH up to 1.o IU/mL.

A hirudin interference study was performed following the same study design as the heparin interference study. Results indicated that Cryo*CHECK*™ Clot S™ may be affected by hirudin and other direct thrombin inhibitors. A statement indicating this has been included under the Limitations of the Procedure section of the package insert.

f. *Assay cut-off:*

2. Comparison studies:

a. *Method comparison with predicate device:*

3 site clinical study in which samples from patients referred for protein S testing were compared to the predicate device. Separate operators and instruments were used at each site. Laboratory A- $y = 0.818x – 6.8$, $n = 115$, $r=0.880$, std error of slope = 13.9; Laboratory B- $y = 0.816x – 5.7$, $n = 120$, $r =0.875$, std error of slope = 14.4; Laboratory C- $y = 0.943x + 3.0$, $n = 46$, $r =0.857$, std error of slope = 18.7;

b. *Matrix comparison:*

3. Clinical studies:

a. Clinical Sensitivity:

b. Clinical specificity:

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

4. Clinical cut-off:

5. Expected values/Reference range: 104 normal (normal PT, normal APTT, normal fibrinogen, neg APC, neg lupus anticoagulant, non medicated) individual donor samples were tested. Ages range from 18-67. 64 males, 40 females, and females were not taking oral contraceptives.

	Males	Females	Total Pop
n	64	40	104
Mean % Protein S	100.1	97.9	99.3
Standard Deviation	27.9	29.5	28.2

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.