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

A. 510(k) Number:

K050365

B. Purpose for Submission:

New Device

C. Measurand:

Protein C

D. Type of Test:

Quantitative

E. Applicant:

Hyphen BioMed

F. Proprietary and Established Names:

Biophen Protein C

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.7290, Factor Deficiency Test

2. Classification:

   Class II

3. Product code:

   GGP, Test, Qualitative and Quantitative Factor Deficiency

4. Panel:

   (81) Hematology

H. Intended Use:

1. Intended use(s):

   Biophen Protein C (5 & 2.5) kit is an in-vitro diagnostic test for the quantitative determination of Protein C in human citrated plasma by chromogenic assay, using a manual or automated method.

2. Indication(s) for use:

   Biophen Protein C is a chromogenic assay for measuring the Protein C activity in human citrated plasma using a manual or automated method.

3. Special conditions for use statement(s):

   Not applicable.

4. Special instrument requirements:

   Not applicable.

I. Device Description:

Biophen Protein C in-vitro diagnostic kit is a chromogenic assay for measuring the Protein C activity in human plasma using a manual or automated method. The kit contains a chromogenic substrate and Protein C activator. The kit is marketed in two sizes, Biophen PC, 5 [4 vials reconstituted to 5ml (200 tests)] and Biophen PC, 2.5 [3 vials reconstituted to 2.5ml (75 tests)].

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Coamatic Protein C

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

   K922201

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Biophen Protein C	***Coamatic® Protein C***
Intended use	Used for measuring the Protein C activity in human plasma by chromogenic assay using a manual or an automated method.	Same
Form	Lyophilized	Same
Matrix	Reagent 1: Protac® in distilled water. Reagent 2: SaPC-21 substrate in distilled water.	Reagent 1: Protein C activator in distilled water. Reagent 2: S-2366 Substrate in distilled water.
Materials	Reagent 1 (Protac®): purified enzyme extracted from the Agkistrodon C Contortrix snake venom, lyophilized. Reagent 2 (SaPC-21): Chromogenic substrate specific for Protein C, lyophilized.	Reagent 1 (Protein C Activator): Lyophilized venom enzyme from southern copperhead snake (Agkistrodon C. Contortrix). Reagent 2 (S-2366): Chromogenic substrate, lyophilized.

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

Not provided.

L. Test Principle:

Protein C is an anticoagulant protein, which is dependant on Vitamin K. It inhibits and regulates coagulation through the specific cleavage of factors Va and VIIIa, suppressing their procoagulant cofactor activity.

Protein C in human plasma is measured following specific activation using Protac®, an enzyme extracted from snake venom (Agkistrodon C Contortrix). The activated protein C (APC) then specifically cleaves the specific substrate SaPC-21, releasing

para-nitroaniline (pNA). The release of para-nitroaniline produces color, which is measured at 405nm. There is direct relationship between release of par-nitroaniline and the protein C activity in the tested plasma.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A reproducibility study was performed on Protein C concentrations of 98%, 59% and 39%. The results are as follows:

Mean Activity	Intra-assay (CV %)	Mean Activity	Inter-Assay (CV %)
98%	0.37% (n=9)	98%	1.26% (n=12)
59%	1.17% (n=10)	59%	1.97% (n=12
39%	0.84% (n=10)	30%	1.51% (n=12)

b. Linearity/assay reportable range:

Linearity was determined using the Protein C calibrator with values of 0, 20, 40, 60, and 100 % activity. The linear regression results for two lots of Biophen Protein C reagent are as follows:

$r^2 = 0.996$ $y = 0.009x + 0.022$
$r^2 = 0.999$ $y = 0.081x + 0.056$

The highest reportable value is 100 %.

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

Stability studies were performed on Protac (R1) and SaPC-21 substrate (R2) vials stored at room temperature (18-25^{o}C) or at 2-8^{o}C, reconstituted. The activity was tested, after storage periods of 1-4 weeks. In addition, they were tested at 3 and 7 months. This study determined that reconstituted R1 and R2 reagents are stable: 3 days at room temperature (18-25^{o}C), 3 months at 2-8^{o}C.

d. Detection limit:

Threshold detection testing was performed using two lots of reagent. The limit of detection was determined to be 5% activity.

e. Analytical specificity:

Not applicable.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:
Comparison studies using the Biophen Protein C assay and the predicate device were performed at two sites with patient samples presented for Protein C testing. The results are as follows:

Site 1	$r^2 = 0.99$	$y = 1.00x + 0.84$	$n = 21$
Site 2	$r^2 = 0.99$	$y = 0.95x + 7.9$	$n = 17$

b. Matrix comparison:

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

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

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The expected range was established in the literature. The 100% Protein C concentration corresponds to the concentration in a normal human citrate plasma pool, obtained by pooling plasma from healthy males or females aged from 18 to 55 years, and out of any medication. The Protein C concentration in adults is usually between 70 and 140%.

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.