

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k091284

B. Purpose for Submission:

To obtain clearance for the VisuCal-F frozen calibrator plasma, VisuCon-F frozen normal control plasma and VisuCon-F frozen abnormal control plasma

C. Measurand:

Normal and Abnormal Control Plasma: Fibrinogen (Clauss Method), coagulation factors II, V, VII, VIII, IX, X, XI and XII, antithrombin activity, protein S activity and protein C activity.

Calibrator plasma: Fibrinogen (Clauss Method), coagulation factors II, V, VII, VIII, IX, X, XI and XII, anti-thrombin activity, α -2-antiplasmin, plasminogen, protein C activity and antigen, protein S activity and total antigen, von Willebrand factor antigen and ristocetin cofactor.

D. Type of Test:

Assayed Controls and Calibrator

E. Applicant:

Affinity Biologicals, Inc.

F. Proprietary and Established Names:

VisuCal-F frozen calibrator plasma
VisuCon-F frozen normal control plasma
VisuCon-F frozen abnormal control plasma

G. Regulatory Information:

1. Regulation section:
21 CFR 864.5425; Multipurpose systems for in vitro coagulation studies
2. Classification:
Class II
3. Product code:
GGN; Plasma, Coagulation Control
JIX; Calibrator, Multi-Analyte Mixture
4. Panel:
Hematology 81

H. Intended Use:

1. Intended use(s):
The VisuCal-F frozen calibrator plasma is intended for use in the calibration of coagulation and fibrinolysis assays.

The VisuCon-F frozen normal control plasma is intended for use in the quality control of coagulation assays in the normal range.

The VisuCon-F frozen abnormal control plasma is intended for use in the quality control of coagulation assays in the borderline pathological range.
2. Indication(s) for use:
The VisuCal-F frozen calibrator plasma is intended for use in the calibration of coagulation and fibrinolysis assays including the following: Fibrinogen (Clauss

Method), Coagulation factors II, V, VII, VIII, IX, X, XI and XII, anti-thrombin activity, α -2-antiplasmin, plasminogen, protein C activity and antigen, protein S activity and total antigen, von Willebrand factor antigen and ristocetin cofactor.

The VisuCon-F frozen normal control is intended for use in the quality control of coagulation assays in the normal range for the following parameters: Fibrinogen (Clauss Method), Coagulation factors II, V, VII, VIII, IX, X, XI and XII, antithrombin activity, protein S activity and protein C activity.

The VisuCon-F frozen abnormal control is intended for use in the quality control of coagulation assays in the borderline pathological range for the following parameters: Fibrinogen (Clauss Method), Coagulation factors II, V, VII, VIII, IX, X, XI and XII, antithrombin activity, protein S activity and protein C activity.

3. Special conditions for use statement(s):

Not Applicable

4. Special instrument requirements:

Not Applicable

I. Device Description:

The VisuCal-F frozen calibrator plasma, VisuCon-F frozen normal control plasma, and VisuCon-F frozen abnormal control plasma are pools of normal citrated human plasma collected from a minimum of 20 donors, buffered with 0.02 M HEPES buffer, dispensed and rapidly frozen.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Dade Behring standard human plasma
 Precision Biologic Reference Check normal control plasma
 Precision Biologic Cryocheck abnormal reference check I & II

2. Predicate K number(s):

k023141
 k013708
 k952624

3. Comparison with predicate:

Similarities			
Item	Device	Predicate	Additional Predicate
Device name	VisuCal-F frozen calibrator plasma (k091284)	Dade Behring Standard Human Plasma (k023141)	Precision Biologic Cryocheck Normal Reference Plasma (k952622)
Intended Use	For use in the calibration of coagulation and fibrinolysis assays	Same	For use in the <i>in vitro</i> quantification of hemostatic parameters in human plasma. May also be used to assign values to in-house collected normal plasma pools or to commercially available unassayed frozen plasma pools.
Matrix	Citrated human plasma	Same	Same
Traceability of	Value assignments	Value assignments	Same

Similarities			
Item	Device	Predicate	Additional Predicate
calibrator plasma	traceable to SSC/ISTH secondary coagulation standard, where available, which is calibrated against WHO International standards	traceable to WHO International standards, where available	
Analytes	Fibrinogen, factors II, V, VII, VIII, IX, X, XI and XII, von Willebrand factor antigen, ristocetin cofactor, protein S activity, protein C activity, anti-thrombin activity, α -2-antiplasmin, plasminogen, Protein C antigen and protein S total antigen	Fibrinogen, factors II, V, VII, VIII, IX, X, XI and XII, von Willebrand factor antigen, ristocetin cofactor, protein S activity, protein C activity, anti-thrombin activity, α -2-antiplasmin, plasminogen	Same

Differences			
Item	Device	Predicate	Additional Predicate
Analytes		Prothrombin time (PT), factor XIII, C-1 inhibitor, Total complement activity	Factor XIII, Free Protein S antigen, antithrombin antigen
Format	Frozen	Lyophilized	Same
Open vial stability	8 hours at 2–8°C except protein S which is stable for 4 hours at 2–8°C	4 hours at 15 to 25°C, 4 weeks at -20°C	8 hours at 2–8°C
Open vial stability	8 hours at 2–8°C		Same
Traceability of calibrator plasma	Value assignments traceable to SSC/ISTH secondary coagulation standard, where available, which is calibrated against WHO International standards		Same
Device Name	VisuCon-F frozen normal control plasma	Precision Biologic Reference Check Normal Control (k013708)	
	VisuCon-F frozen abnormal control plasma	Precision Biologic Abnormal 1 Reference Control (k952624)	
Intended Use	VisuCon-F frozen normal control plasma: For the quality control of coagulation assays in the normal range. VisuCon-F frozen abnormal control plasma: For the quality control of coagulation assays in the borderline pathological range.	Precision Biologic Reference Normal Control: For controlling the accuracy of quantitative hemostasis assays in the normal range. Precision Biologic Abnormal 1 Reference Control: For controlling the accuracy of quantitative hemostasis assays in the normal range.	
Matrix	Citrated human plasma		Same
Format	Frozen		Same
Analytes	Fibrinogen, factors II, V, VII, VIII, IX, X, XI and XII, protein S activity, protein C activity, anti-thrombin activity		Same

Differences		
Item	Device	Predicate
Device Name	VisuCon-F frozen normal control plasma VisuCon-F frozen abnormal control plasma	Precision Biologic reference control normal Precision Biologic abnormal 1 reference control
Analytes		Factor XIII, von Willebrand factor antigen, ristocetin cofactor, Prekallikrein, protein S total antigen, free antigen, protein C antigen, anti-thrombin antigen, α -2-antiplasmin, plasminogen

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

Points to consider: Guidance for Industry and FDA Staff - Assayed and Unassayed Quality Control Material, February 3, 1999.

L. Test Principle:

The VisuCal-F frozen calibrator plasma is an assayed reference plasma prepared from a pool of citrated human plasma collected from a minimum of 20 donors, buffered with 0.02M HEPES buffer, dispensed and rapidly frozen. The plasma can be used to construct a reference curve when measuring the following parameters: Fibrinogen (Clauss Method), coagulation factors II, V, VII, VIII, IX, X, XI and XII, anti-thrombin activity, α -2-antiplasmin, plasminogen, protein C activity and antigen, protein S activity and total antigen, von Willebrand factor antigen and ristocetin cofactor.

The VisuCon-F frozen normal control plasma is a pool of normal citrated human plasma collected from a minimum of 20 donors, buffered with 0.02M HEPES buffer, dispensed and rapidly frozen. This control plasma may be used to confirm assay calibration and to monitor the performance of coagulation assays for the following parameters: fibrinogen (Clauss Method), coagulation factors II, V, VII, VIII, IX, X, XI and XII, anti-thrombin, protein C and protein S.

The VisuCon-F frozen abnormal control plasma is a pool of 20 normal citrated human plasma donors, diluted to defined concentrations, buffered with 0.02M HEPES buffer, dispensed and rapidly frozen. This control plasma may be used to monitor the performance of coagulation assays for the following parameters: fibrinogen (Clauss Method), coagulation factors II, V, VII, VIII, IX, X, XI and XII, anti-thrombin, protein C and protein S.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision testing for the VisuCal-F frozen calibrator plasma and the VisuCon-F frozen normal and abnormal control plasmas was performed as part of the value assignment process by running each lot of plasma in replicates of five over 4 days (n=20). The intra-assay and inter-assay precision results for each analyte were calculated per NCCLS (CLSI) Guideline EP05-A2. Results were

considered valid if predefined acceptance specifications of %CV of $\leq 5\%$ or 15% , depending on the analyte tested, were achieved for intra and inter-assay precision.

b. *Linearity/assay reportable range:*

Not Applicable

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

Traceability: Calibrator value assignment is traceable to SSC/ISTH secondary coagulation standard, where available, which is calibrated against WHO International standards.

Stability: Open-vial stability of the thawed calibrator and control plasmas was performed on two validation lots for each product. After thawing, plasmas were tested for the indicated analytes, stored at $2-8^{\circ}\text{C}$ in the original vial and retested at 4 hours and 8 hours after initial testing. Antigen assays were only performed if activity assays showed a significant decrease over time. Plasmas were considered stable if the following specifications were met:

Results at 4 and 8 hour time points are:

- Within $\pm 10\%$ of the time 0 result for PT and aPTT
- Within $\pm 15\%$ of the time 0 result for fibrinogen, factors II to XII, antithrombin, protein C and protein S

Calibrator Value Assignment: Assigned values for all analytes for each lot of calibrator plasma were determined by testing 20 vials over 4 days, five vials per day and calculating the mean value of the determinations.

Controls Value Assignment: For each lot of normal and abnormal control plasma, ranges were assigned to the various analytes by testing 20 vials over 4 days, five vials per day and calculating the mean ± 2 standard deviations.

d. *Detection limit:*

Not Applicable

e. *Analytical specificity:*

Not Applicable

f. *Assay cut-off:*

Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Not Applicable

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 values for the VisuCal-F Calibrator are demonstrated in the table below.

Parameter		Result	Instrument
Fibrinogen (Clauss) ¹		3.41 g/L	STA Compact
Factor II (activity) ¹		89%	STA Compact
Factor V (activity) ¹		105%	STA Compact
Factor VII (activity) ¹		105%	STA Compact
Factor VIII (activity) ¹ (clotting)		78%	STA Compact
Factor IX (activity) ¹		113%	STA Compact
Factor X (activity) ¹		99%	STA Compact
Factor XI (activity) ¹		99%	STA Compact
Factor XII (activity) ²		118%	STA Compact
α -2- antiplasmin (activity) ³		123%	ACL7000
Antithrombin (activity) ¹		107%	STA Compact
Plasminogen (activity) ³		97%	ACL7000
Protein C	activity ¹	100%	STA Compact
	antigen ¹	100%	Microplate reader
Protein S	activity ¹	102%	STA Compact
	antigen ¹	100%	Microplate reader
vWF	antigen ¹	105%	Microplate reader
	Ristocetin Cofactor ¹	63%	BCS

¹ Calibrated against SSC/ISTH reference standard

² Calibrated against Standard Human Plasma Dade Behring

³ Calibrated against Cryocheck Normal Reference Plasma Precision Biologic

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.