

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE AND INSTRUMENT TEMPLATE**

A. 510(k) Number:

K033137

B. Analyte:

Prothrombin Time, Derived Fibrinogen, INR

C. Type of Test:

Semi-quantitative, Fibrin clot based and photo-optical

D. Applicant:

WADA, Inc.

E. Proprietary and Established Names:

POTENS+

F. Regulatory Information:

1. Regulation section:
21 CFR 864.5425
Multipurpose System for In Vitro Coagulation Studies
2. Classification:
Class II
3. Product Code:
JPA
4. Panel:
Hematology (81)

G. Intended Use:

1. Intended use:
The POTENS+ is a multipurpose system for use in performing clot based, photo-optical in-vitro coagulation studies including Prothrombin Time (PT) derived Fibrinogen (FBG), and the International Normalization Ratio (INR).
2. Indication for use:
The POTENS+ an *in vitro* medical device to determine the coagulation profile of citrated human plasma specimens to be used by a medical professional in a laboratory setting. This profile includes Prothrombin Time (PT) derived Fibrinogen (FBG), and the International Normalization Ratio (INR).
3. Special condition for use statement(s):
Not applicable
4. Special instrument Requirements:
Not applicable

H. Device Description

POTENS+ is a semi-automated system for *in vitro* coagulation studies, utilizing a clot based, photo-optical method. It is an arithmetically linear, digital coagulation device that determines the Prothrombin Time (PT) and calculates the International Normalization Ratio (INR) of a patient's plasma sample. It determines the derived Fibrinogen (FBG) in which the Optical Density (O.D.) change of the optically clear FBG in plasma converts to turbid fibrin clot to determine the FBG content of the specimen. Also, included in this system are two Fibrinogen standards and three Fibrinogen controls.

I. Substantial Equivalence Information:

1. Predicate device name(s):
Organon Tecknika MDA-180 for PT and INR
Organon Tecknika Coag-A-Mate (CAM) MTX for Fibrinogen
2. Predicate K number(s):
K962857, K924453
3. Comparison with predicate:

Similarities			
Item	POTENS+	MDA-180	CAM -MTX
Intended Use	Determine coagulation profile of clinical specimens	Determine coagulation profile of clinical specimens	Determine coagulation profile of clinical specimens
Analytes	PT, FBG, INR	PT, FBG, INR	FBG
Methodology	Fibrin Clot based assay; optical measurement of direct light transmission during clot formation.	Clauss method: Fibrin Clot based assay; optical measurement of relative light transmission to the time of clot formation	Clauss method: Fibrin Clot based assay; optical measurement of relative light transmission to the time of clot formation
Principles of operation	Detects change in light transmittance at 660nm	Detects change in light transmittance in the spectral range 405 to 710nm. FBG @425 & PT @ 580nm	Detects change in light transmittance at 405nm
Method of Detection	Optical (LED with silicon photovoltaic cell	Optical (tungsten lamp) using photodiode detectors	Optical using a photometer and detectors
Target User	Clinical Laboratory	Clinical Laboratory	Clinical Laboratory
Operating Temp	37± 0.3° C	37± 1° C	37
Test Sample	Citrate plasma	Citrate plasma	Citrate plasma
Expression of Results	Fibrinogen: mg/dl PT: seconds INR: INR units	Fibrinogen: mg/dl PT: seconds INR: INR units	Fibrinogen: mg/dl
Differences			
Item	POTENS+	MDA-180	CAM -MTX

Instrument System	Potentiophotometer, Reagent Dispenser, Pipettor, Heating block, computer and printer	Multi-Channel Discrete Analyzer	Analyzer (measuring rotor and photometer), computer and printer
Signal Processing	Linear handling of light transmission using digital electronics	Logarithmic handling of light transmission using analog electronics	Logarithmic handling of light transmission using analog electronics
Reagents/ Accessories	<u>Calibration standards (2)</u> <u>Controls (3)</u> Reagent Water Test Cuvetts Cuvette rack Normal Saline Thromboplastin (Dade® Thromboplastin C Plus)	<u>VeriCal Calibrator Set</u> <u>Verify Controls</u> Reagent Water Buffer Test Cuvetts Clauss Reagents Thrombin, Imidiazole buffer)	Reference Plasma (for calibration) <u>Verify Controls: Veronal Buffer</u> Sample cups Cuvette Rotor Fibriquik (Thrombin)
Test Sample Dilution	None	Required	Required
Reportable Range	FBC: linear range of FBG This is from high to low standards (HS & LS), beyond this to be established by user (99-851 mg/dl obtained in comparative study) PT: 7.1 to 90 seconds INR: ≥ 0.5 with limited clinical utility >4.5 . Upper limit dictated by ISI of thromboplastin used.	FBG II: 35-700 mg/dl depending on dilution set up PT: 8-150 INR 0.8-8.0 with limited clinical utility >4.5	FBG: 40-650 mg/dl depending on dilution set up
Quality Control	Use control plasmas to monitor performance; run once every 55 samples and every 8 hours, whichever occurs first as specified in operators manual.	Use control plasmas and other parameters at frequency and limits specified in operators manual	Use control plasmas and other parameters at frequency and limits specified in operators manual

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

WHO Expert Committee on Biological Standardization 33rd Report; WHO Technical Report Series 687, Geneva, 1983.

EP5-A "Evaluation of Precision Performance of Clinical Chemistry Devices," NCCLS

EP6-P "Evaluation of the Linearity of Quantitative Analytical Methods," NCCLS

EP7-P "Interference Testing in Clinical Chemistry," NCCLS

K. Test Principle:

POTENS+ is an arithmetically linear, digital coagulation instrument that simultaneously determines the Prothrombin time (PT), the International Normalization Ratio (INR) and Fibrinogen (FBG) level in plasma samples.

POTENS+ measures PT and Fibrinogen following the principles of PT-derived methods. When Thromboplastin-Calcium reagent is added to a citrated plasma sample, enzymatic reactions occur leading to the conversion of Prothrombin to Thrombin. Thrombin then converts Fibrinogen to a fibrin clot. POTENS+ detects the beginning of the fibrin clot formation that indicates the PT of the sample. The change in optical density (OD) during fibrin clot formation is detected and compared to the results from similarly treated Fibrinogen standards. POTENS+ detects these OD changes using patented potentiophotometric technology.

POTENS+ directly displays the concentration of the substance being measured because the output of the POTENS+ is inherently linear, in the true digital sense and does not require a logarithmic-linear converting device, circuit, or computers which are required

L. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*

Within-run precision studies were performed according to NCCLS Guideline EP5-A using three levels of control plasma (Control 1, Control 2, and Control 3) and two instruments.

Analyte	Sample	Inst.# 1/2	N	Mean	CV
Fibrinogen	CTL 1	combined	40	322.2	2.8 %
	CTL 2	combined	40	189.7	3.2 %
	CTL 3	combined	40	101.4	5.7 %
PT	CTL 1	combined	40	20.4	10.7 %
	CTL 2	combined	40	11.5	2.8 %
	CTL 3	combined	40	16.7	6.2 %
INR	CTL 1	combined	40	3.1	18.4 %
	CTL 2	combined	40	1.2	6.6 %
	CTL 3	combined	40	2.2	12.3 %

Day to day precision studies were performed according to NCCLS Guideline EP5-A using three levels of control plasma (Control 1, Control 2, and Control 3) and two instruments on at least 20 days.

Analyte	Sample	Inst.# 1/2	Number of days	Number of results	Mean	CV
Fibrinogen	CTL 1	combined	41	82	320.9	4.5%
	CTL 2	combined	41	82	191.5	4.4%
	CTL 3	combined	41	82	106.9	5.6%
PT	CTL 1	combined	41	82	20.5	6.4%
	CTL 2	combined	41	82	11.63	2.3%
	CTL 3	combined	41	82	17.2	4.6%
INR	CTL 1	combined	41	82	3.07	11.0%
	CTL 2	combined	41	82	1.18	5.5%
	CTL 3	combined	41	82	2.28	7.6%

b. *Linearity/assay reportable range:*

The linearity was established according to NCCLS Guideline EP6-P. POTENS+ is designed to be linear from the Low Standard through the High Standard. A plasma pool was spiked with Fibrinogen cryoprecipitate and a portion diluted 1:9 with normal saline.

Mixtures of these two solutions were made to obtain a total of five levels. Four replicates of the five levels were evaluated. The results were compared against the theoretical results. These results indicate that the POTENS+ was linear from 99 to 851 mg/dl. Each laboratory should verify the linearity of the instrument below and above the Standard for each Lot of Standards and Thromboplastin used. Only patient results in the linear range should be reported.

Reportable range:

Method comparison studies were used to verify that the instrument reports results within the range of:

Fibrinogen 136-851 mg/dl
 PT 8.8-41.2 seconds
 INR 0.7-9.9

However, each laboratory should verify the reportable range of each analyte.

c. *Traceability (controls, calibrators, or method):*

Indirect traceability was demonstrated by including plasma fibrinogen (98/614) standard in the Ware-Ratnoff method currently used to determine the Fibrinogen concentration of the POTEN+ Standards. Communication from the NIBSC indicated that the 1st International Standard (IS) (98/614) could be used in the Ratnoff method.

d. *Detection limit:*

The lower detection limit was measured in comparative studies:

Lowest Level measured:

Fibrinogen 79 mg/dl

PT 8.8 seconds (software limit 7.1)

INR 0.7 (INR calculations are limited by the lower PT limit of 7.1 and by the ISI of the thromboplastin used)

e. *Analytical specificity:*

Interference studies were performed by spiking human plasma or plasma pools with bilirubin, hemoglobin, heparin triglycerides, and fibrinogen degradation products. Although bilirubin, hemoglobin and triglyceride showed no affect above the normal range typically found in plasma, visibly icteric, hemolyzed or lipemic specimens should not be used. Heparin at the upper therapeutic range (0.5 Units/ml) affected PT and INR but did not affect Fibrinogen result at the highest level tested (1.7 Units/ml). Fibrinogen Degradation Product digest did not affect the PT or INR results, however, precautions should be taken when analyzing specimens with this elevation until additional studies have been completed determined the level of Fibrinogen Degradation Products that does not cause interference.

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Comparison studies were performed at four sites to demonstrate that POTENS+ is equivalent to the MTX for determining Fibrinogen concentration and to the MDA-180 for determining PT and INR results using a minimum of 200 specimens. Equivalence was demonstrated using commercially available methods/product along with patient specimens covering the normal, therapeutic and diagnostic ranges. Correlation coefficients (r-value) ranged from 0.973 to 0.980 for Fibrinogen, 0.95 to 0.974 for PT and 0.919 to 0.963 for INR results.

b. *Matrix comparison:*

Not reported

3. Clinical studies:

a. *Clinical sensitivity:*

Not provided.

b. *Clinical specificity:*

Not provided.

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

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

From the literature, the generally accepted fibrinogen reference interval is 200mg/dl to 400mg/dl. This is only a guide to the user. Each laboratory should establish specific fibrinogen reference intervals.

M. Instrument Name: POTENS+**N. System Descriptions:**1. Modes of Operation:

Semi-automatic

2. Software:

The POTENS+ software is PC based with the primary responsibility of providing an interface to the user, performing the testing, and handling the results data.

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes or No

3. Sample Identification:

Sample identification is by manual entry. The software accepts input from both a scanner and a keyboard.

4. Specimen Sampling and Handling:

The POTENS+ uses citrate plasma samples and the software controls interface with the pipettor so that the user can transfer the sample to a cuvette.

5. Assay Types:

Clot based assays

6. Reaction Types:

Photo-optical

7. Calibration:

The system includes two Fibrinogen standards. A four standards test is required (2 "high" and 2 "low"). The software shall recognize via the Specimen ID that the standard is being run. If it is the first standard, POTENS+ shall reset all parameters to indicate that a new batch is being started. When the instrument has successfully completed the fourth standard (second low standard) test it will determine the mean values of the PT and the Fibrinogen (FBG) calibration curve. All future FBG calculations for the batch uses this equation.

8. Quality Control:

This system includes three Fibrinogen controls. Whenever the POTENS+ encounters a Specimen ID of CTL1 (Control 1), CTL2 (Control 2) OR CTL3 (Control 2), it regards the test as a control test. The software will use the appropriate maximum/minimum control values from the parameter table to assure that the instrument is properly calibrated. If the checks fail, the software will report the value as "OUT of control." Otherwise, the software will report the value as "In control."

POTENS+ Control 1 is not suitable for use as a control for Prothrombin Time (PT) or INR assays

O. Other Supportive Instrument Performance Characteristics Data Not Covered In The “L. Performance Characteristics” Section Of the SE Determination Decision Summary.

P. Conclusion:

Based upon review of the information and labeling provided, this device is found to be substantially equivalent (SE) to 21 CFR 864.5425 JPA, System, Multipurpose for In Vitro Coagulation Studies, Class II.