

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

A. 510(k) Number:

k071265

B. Purpose for Submission:

New Submission

C. Measurand:

Prothrombin Time Assay with INR

D. Type of Test:

Quantitative

E. Applicant:

Inverness Medical Innovations, Inc.

F. Proprietary and Established Names:

SmartCheck INR™ System

G. Regulatory Information:

1. Regulation section:

864.5425 Prothrombin Time Test

2. Classification:

Class II

3. Product code:

JPA

4. Panel:

H. Intended Use:

1. Intended use(s):

The SmartCheck INR™ System is intended for quantitative testing of Prothrombin Time in capillary blood. Results are given in International Normalize Ratio (INR) units.

The SmartCheck™ INR System is indicated for used by trained medical professionals in a point of care setting for monitoring the INR of patients on oral anticoagulant therapy.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

None

4. Special instrument requirements:

None

I. Device Description:

The SmartCheck™ INR System consists of a hand held battery-powered meter with ROM calibration chip, disposable, dual-chambered, test strips and high and low level external liquid controls. When blood is applied to the strip it migrates by capillary action to the reaction chambers of the strip. The reaction chamber contains a metallic disc and rabbit brain thromboplastin reagent. When blood enters the reaction chamber a magnetic field is applied to the strip to activate disc movement. Upon clot formation, the disc becomes immobilized and clotting is optically detected. Clotting time is calculated and displayed as an INR result.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Diagnostics Corporation CoaguChek® S System, k020831 and k994349

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

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	The SmartCheck INR™ System is intended for quantitative testing of Prothrombin Time in capillary blood. Results are given in International Normalize Ratio (INR) units. The SmartCheck™ INR System is indicated for used by trained medical professionals in a point of care setting for monitoring the INR of patients on oral anticoagulant therapy.	The CaoguChek S System is intended for quantitative Prothrombin Time (PT) testing for monitoring of warfarin therapy, using fresh capillary or non-anticoagulated venous whole blood by professional health care providers.
Measuring Range	0.8-8.0 INR	0.8-7.2 INR
Principle of Operation	Optical detection of thrombin activity resulting from the immobilization of magnetic discs (carbon steel) implanted in the test strip	Optical detection of thrombin activity using iron particles (ferric oxide) that move in a magnetic field
Closed System	Instrument, reagent strips and controls are provided by Inverness and are intended to be used together	Instrument, reagent strips with controls are provided by Roche and are intended to be used together
Quality Controls	Bi-level external liquid controls	External liquid controls and electronic quality control
Test Strip Application	Top fill only	Top dosing only
Calibration	Master reagent lot calibrated to WHO reference rTF/95 (human) and CRM1495 (rabbit) Manual tilt tube method	Master reagent lot traceable to WHO reference rTF/95 Manual tilt tube method

Differences		
Item	Device	Predicate
Sample Volume	≤ 3µL capillary blood	10 µL capillary blood minimum
Thromboplastin	<u>Rabbit brain</u>	Human recombinant
Memory	Stores at least 24 test event. Most recent test event plus 7	60 test results with time and date

Differences		
Item	Device	Predicate
	latest successful test results with date and time are visible on screen	
Power Source	Battery 2 X 1.5v AA LR6 (alkaline Manganese, non-rechargeable)	Battery 4 X 1.5v AA

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

CLSI C28-A2 for Normal Range Study

CLSI-EP7 for Interference Testing

International Reference Preparations (IRP) for calibration

World Health Organization (WHO) for calibration and INR calculation

L. Test Principle:

Blood (or plasma control) is applied to the designated blood collection point on the test strip and migrates by capillary action in dual channels along the length of the strip where each channel ends in a reaction chamber. Each reaction chamber contains a metallic disc and rabbit brain thromboplastin for initiation of the coagulation cascade leading to clot formation. Coagulation is assessed by measuring the clotting time of blood or plasma via a physical system that detects movement of the disc in each of the two chambers of the test strip, movement of the disc starts when the blood reaches the reaction chamber.

The metallic disc is propelled from side-to-side in each chamber by magnetic fields. Disc movement causes mixture of the blood and thromboplastin. Disc movement is monitored optically. When blood enters each of the two chambers, a signal is sent to signify the beginning of the test and the start of timing. As blood reacts with the clotting chemicals, disc movement is impeded. When the disc stops moving the blood is deemed to have clotted and a signal is sent to the meter software to signify the end of the test and end of timing.

The clotting time is measured as the average time taken from entry of the blood until the disc stop moving. The measured PT value is translated to INR.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The total precision was calculated according to EP5-A2 Evaluation of Precision Performance of Quantitative Methods. For each of the 5 days, 10 meters were used to read strips from 2 different batches at 2 levels of control concentration (high and low)

For low control concentration

$$0.10077/0.962 \times 100 = 10.5\%$$

For high control concentration

$$0.61556/3.757 \times 100 = 16.4\%$$

The precision of the system was determined with whole blood samples from 280 patients on Coumadin spanning a wide INR range (as the system was designed) and a precision of 8.7% CV was obtained.

b. *Linearity/assay reportable range:*

0.8 to 7.2 INR

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

Standardized to the International Reference Preparations (IRP) and World Health Organization (WHO)

d. *Detection limit:*

N/A

e. *Analytical specificity:*

N/A

f. *Assay cut-off:*

N/A

2. Comparison studies:

a. *Method comparison with predicate device:*

The SmartCheck INR results obtained on fingerstick capillary whole blood was compared to the ACL 1000 with PT/Fibrinogen reagent, ACL 1000 with PT High Sensitivity Plus reagent, and ACL 1000 with recombinant thromboplastin reagent on aliquots of frozen venous plasma in three laboratory sites.

Summary of Orthogonal Regression Analyses for SmartCheck vs ACL 1000 with recTP

	All Sites Combined	Site 1	Site 2	Site 5
Test Strip Lot	A+B	A	A	B
# Meters	12	3	4	5
N	315	116	82	117
Slope (95% CI)	1.17 (1.07 to 1.27)	1.26 (1.11 to 1.41)	1.04 (0.86 to 1.21)	1.16 (0.96 to 1.37)
Intercept (95%) CI	-0.49 (-0.73 to 0.25)	-0.73 (-1.12 to 0.35)	-0.13 (-0.55 to 0.30)	-0.50 (-.098 to -0.01)
R	0.9235	0.9305	0.9235	0.9205
Sy,x	0.250	0.252	0.253	0.236
Range of x	1.2 to 6.2	1.2 to 6.2	1.3 to 6.2	1.3 to 5.4
Range of y	0.9 to 7.2	.9 to 7.2	1.2 to 6.4	1.1 to 7.1

Summary of Orthogonal Regression Analyses for SmartCheck vs ACL 1000 with PTHS

	All Sites Combined	Site 1	Site 2	Site 5
Test Strip Lot	A+B	A	A	B
# Meters	12	3	4	5
N	310	114	82	114
Slope (95% CI)	1.48 (1.32 to 1.63)	1.49 (1.16 to 1.81)	1.57 (1.33 to 1.81)	1.41 (1.15 to 1.67)
Intercept (95%) CI	-1.19 (-1.57 to -0.81)	-1.26 (-2.07 to -0.45)	-1.38 (-1.97 to -0.80)	-1.00 (-1.67 to -0.40)
R	0.9009	0.9059	0.9065	0.8923
Sy,x	0.247	0.262	0.221	0.247
Range of x	1.2 to 6.6	1.2 to 6.6	1.4 to 4.6	1.2 to 5.0
Range of y	0.9 to 7.2	0.9 to 7.2	1.2 to 6.4	1.1 to 7.1

Summary of Orthogonal Regression Analyses for SmartCheck vs ACL 1000 with PT/FIB

	All Sites Combined	Site 1	Site 2	Site 5
Test Strip Lot	A+B	A	A	B
# Meters	12	3	4	5
N	314	116	82	116
Slope (95% CI)	1.31 (1.21 to 1.42)	1.39 (1.24 to 1.53)	1.37 (1.11 to 1.64)	1.21 (0.99 to 1.43)
Intercept (95%) CI	-0.90 (-1.15 to -0.65)	-1.16 (-1.56 to -0.76)	-1.08 (-1.75 to -0.41)	-0.57 (-1.10 to -0.05)
R	0.9036	0.9135	0.9019	0.8971
Sy,x	0.263	0.266	0.247	0.265
Range of x	1.1 to 6.2	1.1 to 6.2	1.0 to 5.3	1.2 to 5.3
Range of y	0.9 to 7.2	0.9 to 7.2	1.2 to 6.4	1.1 to 7.1

b. *Matrix comparison:*

3. Clinical studies:

a. *Clinical Sensitivity:*

The SmartCheck INR System is sensitive to Factors II, V, VII, and X at the following levels:

Factor II <40% of normal factor level

Factor V <70% of normal factor level

Factor VII <50% of normal factor level

Factor X <60% of normal factor level

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:

Expected values for healthy normal individuals were assessed by the non-parametric method per CLSI 28-A2 on 118 apparently healthy subjects not undergoing oral anticoagulant therapy at three clinical sites (72 females aged 19-58years, 46 males 18-58 years). INR was measured on capillary blood using the SmartCheck INR System on three lots of test strips. The results showed a normal range of 0.8-1.3 INR.

N. Instrument Name:

SmartCheck INR™ System

O. System Descriptions:

1. Modes of Operation:

The SmartCheck™ INR System consists of a hand held battery-powered meter with ROM calibration chip, disposable, dual-chambered, test strips and high and low level external liquid controls. When blood is applied to the strip it migrates by capillary action to the reaction chambers of the strip. The reaction chamber contains a metallic disc and rabbit brain thromboplastin reagent. When blood enters the reaction chamber a magnetic field is applied to the strip to activate disc movement. Upon clot formation, the disc becomes immobilized and clotting is optically detected. Clotting time is calculated and displayed as an INR result.

2. Software:

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

Yes ____X____ or No _____

3. Specimen Identification:

None

4. Specimen Sampling and Handling:

Capillary whole blood

5. Calibration:

Each box of SmartCheck INR Test Strips contains a Calibration Chip. The Calibration Chip contains specific information regarding that lot of Test Strips which is required by the meter to calculate and INR value.

6. Quality Control:

Two levels of external quality control material

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The “Performance Characteristics” Section above:

Q. Proposed Labeling:

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

R. Conclusion:

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

