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

I Background Information:

A 510(k) Number

K251564

B Applicant

iLine Microsystems S.L.

C Proprietary and Established Names

microINR System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
GJS	Class II	21 CFR 864.7750 - Prothrombin Time Test	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

Expansion of measuring range and removal of the Left Ventricular Assist Device (LVAD) limitation.

B Measurand:

International Normalized Ratio (INR)

C Type of Test:

Microfluidic technology with machine vision detection

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The microINR System measures prothrombin time (PT) expressed in International Normalized Ratio (INR), for monitoring oral anticoagulant therapy with warfarin.

The microINR System consists of a meter and chips (test strips) and uses fresh capillary whole blood from a fingerstick.

The microINR System is intended for patient self-testing use as well as for healthcare professionals at Point of Care settings.

The microINR System is intended for use in patients 18 years old or older. Patients must be stable on warfarin medication for at least 6 weeks before starting to use the microINR System.

For Self-testing use: The system is intended for properly trained users under specific prescription of a physician.

Caution: The microINR System is not intended for use in patients who are transitioning from heparin treatment to VKA therapy. The microINR System is not intended to be used for screening purposes.

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:

microINR Expert Meter

IV Device/System Characteristics:

A Device Description:

The microINR System is comprised of a portable measuring device (microINR Expert Meter) and test strips (microINR Chips) in which the capillary blood sample flows through capillary action. The microINR Chip contains a reagent in dried form which consists of thromboplastin, and contains two symmetrical regions, the measuring channel, and a control channel. The microINR Expert Meter measures International Normalized Ratio (INR) based on a prothrombin time (PT) assay carried out in the microINR Chip based on microfluidic technology with machine vision detection.

The microINR System has a multi-level on-board quality control. The microINR Control contains lyophilized human citrated plasma from healthy donors modified by means of a process to simulate an abnormal coagulation sample and a calcium chloride solution. The lyophilized plasma must be reconstituted with the calcium chloride solution before use.

The changes to the microINR Expert Meter include the expansion of the analytical measuring range up to INR of 8.0 and the removal of the LVAD limitation. The modifications have no impact on fundamental scientific technology and its performance.

B Principle of Operation:

The microINR System is a handheld in vitro diagnostic medical device that uses microfluidic technology with machine vision detection to measure the prothrombin time from a fresh capillary (fingerstick) whole blood sample. The fresh capillary (fingerstick) whole blood sample is applied to the microINR Chip (test strip) for testing. The microINR Chip is inserted into the analyzer. Inside the test strip, the applied blood sample is separated into two channels and mixed with the reagents contained in each micro-reactor. The coagulation cascade is triggered instantly after mixing with the reagents (start time of the Prothrombin Time assay). When the blood coagulates its viscosity increases due to fibrin clot formation, which generates a sharp change in blood flow behavior. The Prothrombin Time measures how long it takes to form the fibrin clot after tissue thromboplastin has been added to the sample. The microINR Meter measures the INR based on the Prothrombin Time assay carried out in the microINR Chip and displays the INR on the screen.

C Instrument Description Information:

1. Instrument Name:

   microINR Expert Meter

2. Specimen Identification:

   Barcode scanner or keyboard for manual entry

3. Specimen Sampling and Handling:

   Capillary fingerstick

4. Calibration:

   Automatic, encoded on disposable chip, no end user input

5. Quality Control:

   Multi-level on-board quality controls

V Substantial Equivalence Information:

A Predicate Device Name(s):
microINR System, microINR System

B Predicate 510(k) Number(s):
K243543, K180780

C Comparison with Predicate(s):

Device & Predicate Device(s):	K251564	K243543	K180780
Device Trade Name	microINR System	Same	microINR System
General Device Characteristic Similarities			
Intended Use/Indications For Use	The microINR System measures prothrombin time (PT) expressed in International Normalized Ratio (INR), for monitoring oral anticoagulant therapy with warfarin. The microINR System consists of a meter and chips (test strips) and uses fresh capillary whole blood from a fingerstick. The microINR System is intended for patient self-testing use as well as for healthcare professionals at Point of Care settings. The microINR System is intended for use in patients 18 years old or older. Patients must be stable on warfarin medication for at least 6 weeks before starting to use the microINR System. For Self-testing use: The System is intended for properly trained users under specific prescription of a physician. Caution: The microINR System is not intended for use in patients who are transitioning from heparin treatment to	Same	The microINR System (consisting of the microINR Meter and the microINR Chip) is intended for multiple-patient use by professional healthcare providers for the determination of International Normalized Ratio (INR), to monitor Oral Anticoagulation Therapy (OAT) with warfarin. The microINR system uses fresh capillary whole blood. The microINR System is intended for in vitro diagnostic use at the point-of-care. The microINR System is intended for use in patients 18 years of age and older. Patients must be stabilized (≥6 weeks) on warfarin. Caution: The microINR System is not intended for use in patients who are transitioning from heparin treatment to warfarin therapy. The microINR System is not intended to be used for screening purposes.

	VKA therapy. The microINR System is not intended to be used for screening purposes.		
Sample type	Capillary whole blood.	Same	Same
Operating Principle/Technology	Microfluidic technology with machine vision detection.	Same	Same
Test Strip Reagent	Human recombinant thromboplastin	Same	Same
Calibration traceability	Each lot of test strips is calibrated to a reference lot traceable to the WHO International Reference Preparation.	Same	Same
Reference Range	INR: 0.8 to 1.2	Same	Same
Calibration	Automatic, encoded on disposable, no end user input possible.	Same	Same
Test Strip Stability	15 months.	Same	Same
Test Strip Use Time	6 hours. (Limited to 15 minutes in IFU).	Same	6 hours
Sample Volume	A minimum of 3 µL.	Same	Same
On-Board Quality Control	Multi-level on-board quality controls.	Same	Same
General Device Characteristic Differences			
Measuring Range	0.8 – 8.0 INR	0.8 – 6.0 INR for professional use*. 0.8 – 4.5 INR for self-testing use. (* INR visualization up to 4.5. Both uses commercialized under the same reference)	0.8 – 6.0 INR for professional use NA for self-testing
Software	Remains the same as K243543 but INR upper range up to 8.0.	INR range to 4.5	INR range to 8.0
Limitations of POC settings	The microINR System is intended to be used in Point of Care settings such as physicians' offices and	Same	No limitations

	anticoagulation clinics, as well as home settings. It is not intended to be used in nursing homes, emergency rooms or intensive care units.		
LVAD Patients	No interference observed.	Excluded	Same

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3 – *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline* – Third Edition.

CLSI H21-A5. *Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays;* Approved Guideline-Fifth Edition.

CLSI H54-A. *Procedures for Validation of INR and Local Calibration of PT/INR Systems*; Approved Guideline.

ANSI AAMI ISO 14971:2019. Medical Devices- Applications of risk management to medical devices.

IEC 62304:2006/AMD1:2015 Medical device software - Software life cycle processes.

IEC 60601-1-2:2014 Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests.

IEC 60601-1-2:2014/AMD1:2020 Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests.

IEC 60601-4-2:2024. Medical electrical equipment - Part 4-2: Guidance and interpretation - Electromagnetic immunity: performance of medical electrical equipment and medical electrical systems.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   The reproducibility and intermediate precision of the microINR System is maintained from K180780 and K201185 for INR detection up to 4.5.

A repeatability study was performed to access the precision of the microINR System above INR of 4.5. The repeatability study was performed at three Point of Care (POC) sites designed to simulate the Home Use setting. The study tested paired capillary samples collected and tested by 15 untrained patient self-testers (PST) on warfarin. The same 15 patients had paired capillary samples collected and tested by healthcare professionals (HCP). A total of four microINR Meters and two microINR Chip lots were included in the study. All test results met the pre-defined acceptance criteria. The Table below summarizes the repeatability study results.

Repeatability Summary				
	No. of Test Pairs	**Mean INR**	**SD (95% CI)**	**% CV (95% CI)**
PST	13	5.64	0.26 (0.18, 0.38)	4.6 (3.3, 7.1)
HCP	14	5.35	0.28 (0.16, 0.36)	5.2 (2.8, 6.4)

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Refer to K180780.

4. Assay Reportable Range:

   The assay reportable range of the microINR System was established through analytical studies and the method comparison studies. The reportable range for INR is 0.8–8.0.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Each lot of microINR Chips is factory calibrated to a reference lot of human recombinant thromboplastin traceable to the World Health Organization International Reference Preparation. Separate microINR Chip lots manufactured by iLine Microsystems have been calibrated using the rTF/09 (WHO 4th International Standard Thromboplastin, Human, Recombinant, Plain) and the rTF/16 (WHO 5th International Standard Thromboplastin, Human, Recombinant, Plain).

6. Detection Limit:

   Refer to K180780.

7. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison:

A method comparison study was performed to evaluate the performance of the microINR System above INR of 4.5. The method comparison study was performed at three sites. The study was conducted with four microINR Meters and two microINR Chip lots. A venipuncture was performed for INR determination on the reference analyzer (ACL TOP 750 (K242127) with HemosIL RecombiPlasTin 2G (K070005)) and for the hematocrit assessment. After confirming subjects INR was > 4.5, subjects were enrolled in the study. The enrolled subjects had two paired capillary samples collected by an HCP and tested on the candidate device. 13 of the subjects enrolled self-collected and self-tested two paired capillary samples on the candidate device. To support the INR range expansion, a pooled analysis was performed using method comparison data from K180780 and K201185 and the above-mentioned method comparison study (n=1,016) for the regression analysis. All test results met the pre-defined acceptance criteria. The Table below summarizes the combined method comparison study results.

INR Range	Sample Number	Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)
INR < 4.5	946	1.01 (1.00, 1.03)	0.05 (0.03, 0.08)	0.96
INR ≥ 4.5	70	0.87 (0.74, 1.05)	0.43 (-0.48, 1.14)	0.87

Data analysis was performed to evaluate the effect of disease states and conditions of patients in POC settings that could interfere with the microINR System device. A review of 17 patients enrolled in the method comparison study performed in K180780 with Left Ventricular Assist Devices (LVAD) was performed to demonstrate the accuracy of the microINR System in this subpopulation. As in K180780, with the data from the method comparison study, the effect of the LVAD condition in the microINR System has been analyzed and the microINR System demonstrates acceptable performance when compared to the predicate (Coaguchek XS, K062925) and the reference method (Instrumentation Laboratory ACL TOP 500 laboratory analyzer, K160276 using HemosIL RecombiPlasTin 2G, K070005).

Condition	N	Candidate vs Predicate		Candidate vs Reference Method	
		%Bias	%SD of Bias	%Bias	%SD of Bias
LVAD	17	-5.28	13.15	0.32	10.63

2. Matrix Comparison:

Refer to K180780.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Refer to K180780.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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