510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K201185

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:

Expand Intended Use to include home users

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.

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
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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 microINR® Meter and microINR® Chip 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 Meter

IV Device/System Characteristics:

A Device Description:

The microINR System is comprised of a portable measuring device (microINR 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 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. Multiple key functions and elements of the system are checked and if deviations are detected, error messages are displayed and test results are not reported.

B Principle of Operation:

The microINR System was previously cleared for professional use under premarket notification K180780. The test principle has not been modified:

The microINR System is a closed system, which is intended to be used exclusively with the microINR Chips manufactured by iLine Microsystems, S.L. 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 Chips (test strips) for testing. The microINR Chip is inserted into the analyzer. Two microcapillary channels in the test strip are filled with the blood sample by capillary action. The microINR Chip contains a preparation of human recombinant tissue factor, synthetic phospholipids and stabilizers. The microINR Meter measures the International Normalized Ratio (INR) based on the Prothrombin Time (PT) assay carried out in the microINR Chip and displays the International Normalized Ratio (INR) on the screen.

C Instrument Description Information:

1. Instrument Name:

   microINR System

2. Specimen Identification:

   Manual entering of patient identification

3. Specimen Sampling and Handling:

   The microINR Chip is intended for single-use only. Once the Chip is inserted into the device, a drop of fresh capillary whole blood sample collected by fingerstick is manually applied to the Chip and analyzed by the microINR Meter.

4. Calibration:

   Each lot of microINR Chips is calibrated to a reference lot of human recombinant thromboplastin traced to International Reference Thromboplastin of the World Health Organization.
   These calibration parameters (International Sensitivity Index (ISI) and Mean Normal Prothrombin Time (MNPT)) are encoded in the printed Datamatrix of each microINR Chip along with information related to expiration date. Therefore, every test is automatically and individually calibrated eliminating risk of human error.

5. Quality Control:

   The microINR System provides both the Meter´s functional Quality Controls and On-Board Quality Controls.
   First, Meter performance is automatically checked for electronic components, correct power battery level and environmental temperature conditions.
   Then, On-Board Controls provide a quality control check for each individual microINR Chip used with the microINR Meter. The microINR System has been designed to detect errors prior to and during the test in order to prevent inaccurate INR results through a multi-level strategy.

V Substantial Equivalence Information:

A Predicate Device Name(s):

microINR System

B Predicate 510(k) Number(s):

K180780

C Comparison with Predicate(s):

Device & Predicate Device(s):	K201185	K180780
Device Trade Name	microINR System	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 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.	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.

Test Strip Reagent	Human recombinant thromboplastin	Same
Test Strip Stability	15 months	Same
Test Strip Use Time	6 hours (Limited to 15 minutes as per labeling)	6 hours
Operating Principle/Technology	Microfluidic technology with machine vision detection	Same
Calibration Traceability	Each lot of test strip is calibrated to a reference lot traceable to the WHO International Reference Preparation	Same
Calibration	Automatic, encoded on disposable, no end user input possible	Same
Traceability	WHO International Reference Preparation	Same
On-Board Quality Control	Multi-level on-board quality control	Same
Sample Type	Capillary whole blood	Same
Minimum Sample Volume	3 µL	Same
Hemoglobin	No significant effect up to 1000 ng/dL	Same
Hematocrit Range	25–55%	Same
Bilirubin	Up to 40 mg/dL	Same
Triglyceride	Up to 3270 mg/dL	Same
Heparin	Use excluded as per labeling	Same
Low Molecular Weight Heparin	Use excluded as per labeling	Same
Measuring Range	0.8–6.0 INR	Same
Reference Range	0.8–1.2 INR	Same
Operating Temperature	15–35 ˚C (59–95 ˚F)	Same
Expiration Data Lock Out	Automatic, encoded on disposable, no end user input possible	Same
General Device Characteristic Differences		
Limitations of POC Settings	The microINR System is intended to be used in Point of Care settings such as physicians' offices and anticoagulation clinics, as	No limitations

	well as home settings. It is not intended to be used in nursing homes, emergency rooms or intensive care units.	
External Liquid Quality Control	Not available	External optional liquid quality controls
EMC testing	IEC 60601-1-2:2014 (ESD testing 8kV contact and 15kV air discharges)	IEC 60601-1-2:2007 (ESD testing 6kV contact and 8kV air discharges)
Software	Date format: year with 4 digits Error message E13 (control for chip US vs ROW models)	Date format: year with 2 digits No E13 available

VI Standards/Guidance Documents Referenced:

- ANSI/AAMI ES60601-1 Medical electrical equipment – Part 1: General requirements for safety and essential performance
- ANSI/AAMI IEC 60601-1-2 Medical Electrical Equipment - Part 1-2: General Requirements For Basic Safety And Essential Performance - Collateral Standard: Electromagnetic Disturbances - Requirements And Tests
- IEC 60601-2-37 Medical Electrical Equipment - Part 1-6: General Requirements For Basic Safety And Essential Performance - Collateral Standard: Usability
- IEC 60601-1-11:2010 Medical electrical equipment - Part 1-11: General requirements for basic safety and essential performance - Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment
- IEC 62304 Medical Device Software - Software Life Cycle Processes
- Format for Traditional and Abbreviated 510(k)s. Guidance for Industry and Food and Drug Administration Staff
- Design Considerations for Devices Intended for Home Use, Guidance for Industry and Food and Drug Administration Staff
- Content of Premarket Submissions for Management of Cybersecurity in Medical Devices. Guidance for Industry and Food and Drug Administration Staff

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The repeatability study was performed at four point-of-care (POC) sites, with one lot of microINR Chips, eight microINR Meters and at least two operators per site. Enrolled patients visited the POC site twice. At each visit, enrolled patients and the operators performed

duplicate measurements. The precision of duplicates was calculated for both the subjects and POC operators. The precision results were calculated by each visit as well as overall. The result met the pre-defined acceptance criteria.

	Visit 1		Visit 2		Overall	
	User Results	Operator Results	User Results	Operator Results	User Results	Operator Results
N	103	110	110	109	213	219
Mean	2.54	2.55	2.61	2.61	2.58	2.58
SD	0.15	0.11	0.13	0.12	0.14	0.12
CV	5.9	4.3	5.0	4.6	5.4	4.7

2. Linearity:

   Refer to K180780

3. Analytical Specificity/Interference:

   Refer to K180780

4. Assay Reportable Range:

   The assay reportable range (0.8 – 4.5 INR) of the microINR System was established through the Home Use study against the reference laboratory method (Instrumentation Laboratory ACL TOP 500 (K160276) with HemosIL RecombiPlasTin 2G Reagent (K070005)).

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

   Refer to K180780

6. Detection Limit:

   Refer to K180780

7. Assay Cut-Off:

   Not applicable

8. Accuracy (Instrument):

   Not applicable

9. Carry-Over:

   Not applicable

B Comparison Studies:

1. Method Comparison with predicate device:

   The method comparison study was submitted, reviewed and cleared under K180780.

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):

   A Home Use (self-testing) Study was performed at four point-of-care (POC) sites, where a total of 117 eligible subjects (patients stabilized on warfarin therapy and 18 years of age and older) were enrolled. The home use study was conducted with two microINR Meters per site and one lot of microINR Chips. Enrolled patients visited the POC site twice. At each visit, enrolled patients and the health care professionals alternately performed duplicate measurements. In addition, a venipuncture was performed at the second visit for INR determinations on the reference laboratory method (ACL TOP 500 with HemosIL RecombiPlasTin 2G) and the hematocrit assessment. The results obtained by trained users were compared with those obtained by health care professionals as well as the reference laboratory method. Passing-Bablok regression analysis was performed to assess the accuracy of the microINR measurements obtained by patients against results obtained by the health care professionals and the results from the reference laboratory method. All results met the pre-defined acceptance criteria.

   Summary table of the Passing-Bablok regression of patient (PST) and health care professional (HCP) against the reference method

	N	Slope (95% CI)	Intercept (95% CI)	Pearson (r)
PST	112	0.95 (0.86 – 1.05)	0.12 (-0.11 – 0.34)	0.922
HCP	111	0.95 (0.88 – 1.02)	0.15 (-0.04 – 0.32)	0.95

   Summary table of predicted bias (%) at medical decision points for patient (PST) and health care professional (HCP) against the reference method

%Bias	INR=2.0 (95% CI)	INR=3.5 (95% CI)	INR=4.5 (95% CI)
PST	1.2 (-1.5 – 4.5)	-1.4 (-4.7 – 1.9)	-2.1 (-6.5 – 2.6)
HCP	1.9 (-0.4 – 4.9)	-1.2 (-3.5 – 1.4)	-2.2 (-5.1 – 1.5)

Summary table of the Passing-Bablok regression of patient (PST) against health care professional (HCP)

	Slope (95% CI)	Intercept (95% CI)
Overall	1.00 (1.00 – 1.00)	0.00 (0.00 – 0.00)
Visit 1	1.00 (1.00 – 1.11)	0.00 (-0.26 – 0.00)
Visit 2	1.00 (0.95 – 1.00)	0.00 (-0.10 – 0.09)

Summary table of predicted bias (%) at medical decision points for patient (PST) against health care professional (HCP)

%Bias	INR=2.0 (95% CI)	INR=3.5 (95% CI)	INR=4.5 (95% CI)
Overall	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)	0.0 (0.0 – 0.0)
Visit 1	0.0 (-5.0 – 0.0)	0.0 (-2.9 – 3.8)	0.0 (-2.2 – 5.4)
Visit 2	0.0 (-5.0 – 0.0)	0.0 (-2.9 – 0.0)	0.0 (-3.1 – 0.0)

Self-testers enrolled in the study also participated in a questionnaire to survey the usability of the microINR System. On a scale of 1 to 5 where 1 is least favorable and 5 is most favorable, the mean score was 4.69.

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Refer to K180780

F Other Supportive Instrument Performance Characteristics Data:

The On-Board Quality Control (QC) System of the microINR System was validated for analyzing the effect of short sample application and different incorrect sample application methods including sample perturbation and intermittent applications. For each tested condition, clinical samples were collected to test the microINR System performance. A total of 55 fresh venous whole blood samples were obtained from 18 normal subjects and 37 patients under vitamin K antagonist (VKA) therapy with INR ≤ 4.5. Immediately after sample collection, the hematocrit level of patients was measured using the Mission Plus Hb Hemoglobin Testing System. The INR value was determined by the CoaguChek XS System to classify the samples in the required INR ranges.

To assess short sample detection, blood samples with different reduced volumes were measured on the microINR System.

A sample perturbation study was performed to assess the effect of potentially reducing the volume of the applied sample. The remnant of the drop was absorbed using a piece of paper once the measurement started.

An intermittent sampling study was conducted by applying a short sample volume to the microINR Chip, and once the INR measurement began, adding more sample volume before the

INR measurement was complete. It was performed by using different application modes simulating different real-life misuse situations.

All results for tested fault condition met the pre-defined acceptance criteria, demonstrating the adequate performance of the microINR System under different types of incorrect sample application, including short sample, sample perturbation and intermittent sampling application.

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.