January 25, 2019

iLine Microsystems S.L.
Alberto Molinero
Regulatory Affairs and Quality Manager
Paseo Mikeletegi, 69
20009 Donostia, Guipúzcoa
Spain

Re: K180780
Trade/Device Name: microINR System
Regulation Number: 21 CFR 864.7750
Regulation Name: Prothrombin time test
Regulatory Class: Class II
Product Code: GJS, GGN
Dated: March 22, 2018
Received: March 26, 2018

Dear Alberto Molinero:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal

statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Leonthena R. Carrington -S

Lea Carrington
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K180780

Device Name
microINR System
microINR Control Level A
microINR Control Level B

Indications for Use *(Describe)*

microINR System:

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) 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.

The microINR chips are only intended to be used with the microINR meter.

microINR Control Level A / microINR Control Level B:

The microINR Control is intended for quality control performed on the microINR Meter when used with the disposable microINR Chips.

iLine Microsystems has available two microINR Control Levels (A and B) to perform quality control checks in the therapeutic range on the microINR System.

The microINR Control is intended for professional use only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

This 510(k) summary is being submitted in accordance with the requirements of 21 CFR 807.92.

1. SUBMITTER INFORMATION

Owner	iLine Microsystems, S.L. Paseo Mikeletegi, 69 20009 Donostia, Guipúzcoa Spain
Contact	Alberto Molinero amolinero@ilinemicrosystems.com Tel. +34 943 008 733 Fax: +34 943 008 737
Date Summary Prepared	January 18, 2019

2. DEVICE INFORMATION

Proprietary Name	microINR® System microINR® Control Level A microINR® Control Level B
Common Name	Prothrombin time test
Panel	Hematology

Regulatory Information:

Classification				
Device	**Regulation Section**	**Device Class**	**Product Code**	**Test**
microINR® System	21 CFR 864.7750	II	GJS	Prothrombin time test
microINR® Control Level A microINR® Control Level B	21 CFR 864.5425	II	GGN	Plasma, coagulation control

3. SUBSTANTIAL EQUIVALENCE INFORMATION:

Element	Predicate Device
Predicate Device Name	CoaguChek® XS System
Common Name	Prothrombin time test
510 (k) Number	k060978
Manufacturer	Roche Diagnostics

4. 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.

In addition to the microINR® On-Board Controls, the microINR® Control has been developed as an optional liquid quality control solution. The microINR® Control must be used only by healthcare professionals in order to meet the regulatory compliance requirements applicable to the facility where they are to be used.

The microINR® Control contains lyophilized human citrated plasma from healthy donors (not heparinized plasma or plasma samples under oral anticoagulant therapy) modified by means of a dedicated process to simulate an abnormal coagulation sample and a calcium chloride solution. Before use, the lyophilized plasma must be reconstituted with the calcium chloride solution.

5. INDICATIONS FOR USE/INTENDED USE:

Intended Use of the microINR® System:
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) 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.
The microINR® Chips are only intended to be used with the microINR® Meter.

Intended Use of the Optional Liquid Control:
The microINR® Control is intended for quality control performed on the microINR® Meter when used with the disposable microINR® Chips.
iLine Microsystems has available two microINR® Control Levels (A and B) to perform quality control checks in the therapeutic range on the microINR® System.
The microINR® Control is intended for professional use only.

6. SUMMARY COMPARISON OF TECHNOLOGICAL CHARACTERISTICS (PREDICATE):

The following table compares the microINR® System with its predicate device, CoaguChek® XS System (k060978).

Similarities		
Item	**microINR® System**	**CoaguChek® XS System (Predicate)**
Intended Use/Indications for Use	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) 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. The microINR® Chips are only intended to be used with the microINR® Meter.	The CoaguChek® XS system is intended for the use by professional healthcare providers for quantitative prothrombin time testing to monitor warfarin therapy, using fresh capillary or non-anticoagulated venous whole blood.

Similarities		
Item	**microINR® System**	**CoaguChek® XS System (Predicate)**
Sample type	Capillary whole blood.	Capillary or non-anticoagulated venous whole blood.
Test Strip Reagent	Human recombinant thromboplastin.	Same.
Measuring Range	0.8 – 6.0 INR.	0.8 – 8.0 INR.
Hematocrit Range	Hematocrit ranges between 25-55% do not significantly affect test results.	Same.
Hemoglobin	No significant effect up to 1000 mg/dL.	Same.
Calibration traceability	Each lot of test strips is calibrated to a reference lot traceable to the WHO International Reference Preparation.	Same.

Differences		
Item	**microINR® System**	**CoaguChek® XS System (Predicate)**
Operating Principle/Technology	Microfluidic technology with machine vision detection.	Electrochemical technology with amperometric (electric current) detection of thrombin activity
Test Strip Use Time	6 hours.	10 minutes.**
Test Strip Stability	15 months.	21 months.
Operating Temperature	15 – 35ºC (59 – 95°F).	15 – 32ºC (59 – 90°F).**
Minimum Sample Volume	A minimum of 3 µL.	A minimum of 8 µL.*
On-Board Quality Control	Multi-level on-board quality controls.	On-board fully integrated quality controls which use electrochemical signals to detect test strip integrity.
External Liquid Quality Control	External optional liquid quality control: The microINR® Control is intended for quality control performed on the microINR® Meter when used with the disposable microINR® Chips. iLine Microsystems has available two microINR® Control Levels (A and B) to perform quality control checks in the therapeutic range on the microINR® System. The microINR® Control is intended for professional use only.	No external liquid quality control.**

Differences		
Item	**microINR® System**	**CoaguChek® XS System (Predicate)**
Memory Capacity	199 (results with time and date.)	300 test results with date and time. **
Bilirubin	Bilirubin up to 40 mg/dL has no significant effect on test results.	No significant effect up to 30 mg/dL.
Triglyceride	Lipemic samples containing up to 3270 mg/dL of triglycerides have no significant effect on test results.	No significant effect up to 500 mg/dL.
Heparin	Use excluded in IFUs.	Unaffected by heparin concentrations up to 0.8 U/mL.
Low Molecular Weight Heparin	Use excluded in IFUs.	Insensitive to low molecular weight heparins up to 2 IU anti-factor Xa activity/mL.
Reference Range	INR: 0.8 to 1.2.	INR: 0.9 to 1.1.
Calibration	Automatic, encoded on disposable, no end user input possible.	Lot specific code chip selected by end user.
Expiration date lock out	Automatic, encoded on disposable, no end user input possible.	Lot specific code chip selected by end user.

* CoaguChek® XS PT Test Instructions for Use (2017-09).
** CoaguChek® XS System User Manual (2016-08 USA).

7. STANDARD/GUIDANCE DOCUMENT REFERENCED:

CLSI EP05-A3 – Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition
CLSI EP09-A3 – Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition
CLSI EP07-A2 – Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition
CLSI EP25-A – Evaluation of Stability of In Vitro Diagnostic. Reagents; Approved Guideline – First Edition
CLSI EP28-A3c – Defining, Establishing, and Verifying. Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition
CLSI H47-A2 – One-Stage Prothrombin Time (PT) Test and Activated Partial Thromboplastin Time (APTT) Test; Approved Guideline – Second Edition
CLSI H54-A – Procedures for Validation of INR and Local Calibration of PT/INR Systems; Approved Guideline – First Edition

8. TEST PRINCIPLE

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.

9. PERFORMANCE CHARACTERISTICS

The following internal performance data were provided in support of the substantial equivalence determination:

9.1. Analytical Performance

a) Precision/Repeatability:

Repeatability

The repeatability study was performed at three clinical sites, testing capillary samples from normal subjects and patients on warfarin therapy. Multiple Chip

lots, Meters and Operators were included in the study. Two capillary samples (two fingersticks) were collected from each subject resulting into a total of 269 paired tests.

Summary of repeatability for microINR® System

Analysis per INR range	n test pairs	SD	CV%
INR < 2.0	91	0.06	5.25
2.0 ≤ INR < 3.5	129	0.12	4.57
3.5 ≤ INR < 4.5	32	0.21	5.64
INR ≥ 4.5	17*	0.26	5.46

*4 of these values were between 6.0 and 8.0.

b) Reproducibility/Intermediate Precision:

Device reproducibility

The study was performed using two levels of plasma samples. INR was determined in both plasma samples by each device each day.

Device reproducibility data for high abnormal INR level plasma

	N	Mean	Within-Run		Between-Run		Between-Day		Between-Device		Within-Device		Device Reproducibility	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
All Devices	90	3.45	0.16	4.7	0.04	1.0	0.09	2.7	0.00	0.0	0.19	5.5	0.19	**5.5**

Reproducibility data for low abnormal INR level plasma

	N	Mean	Within-Run		Between-Run		Between-Day		Between-Device		Within-Device		Device Reproducibility	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
All Devices	90	2.25	0.11	4.9	0.05	2.0	0.00	0.0	0.03	1.4	0.12	5.3	0.12	**5.5**

c) Linearity/assay reportable range:

A linearity study is not applicable for the microINR® System.

The assay reportable range (0.8 - 6.0 INR) of the microINR® System was established through method comparison studies against the reference device (Instrumentation Laboratory ACL TOP® 500 laboratory analyzer). HemosIL® RecombiPlasTin 2G Reagent was used for prothrombin time (PT) determinations. Data collected across the assay reportable range from the method comparison studies were used to demonstrate linearity on the microINR® System.

d) Traceability, stability, expected values (controls, calibrators, or methods):

Traceability

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.

microINR® Chips Stability

Real Stability: The stability of 15 months shelf life was established by storing three microINR® Chip lots at 25 ºC (77 ºF) (60% Relative Humidity (RH)) and testing using fresh whole blood samples.

In-Use Stability: In-use stability was tested to prove that the microINR® Chips can be kept outside the pouch before measurement for at least 6 hours when directly exposed to 35 °C (95 ºF), 80 % relative humidity RH. It was assessed by exposing the Chips out of their pouches to 35ºC (95 ºF), 80% RH storage and testing using fresh whole blood samples.

Transport Stability: microINR® Chips and its package were validated by a transport stability study. Package evaluation was assessed and the performance of the microINR® Chips was tested using fresh whole blood samples.

Optional Liquid Controls Stability

Stability: The stability of the microINR® Controls is 12 months stored at refrigerated conditions of 2-8 °C according to the data projected from an accelerated study performed with one lot of each microINR® Control level stored at 24.0 °C ± 1.1 °C (75.2 °F ± 34.0 °F) for up to 106 days. The in-use stability of the microINR® Controls is 10 minutes (upon reconstitution) at room temperature (15-25 °C, 59-77 °F).

Target Assignment: The target assignment is performed by using at least 10 vials of each microINR® Control lot performing two runs per day during

several days. A total of 30 duplicated tests are used to determine the mean INR determination (target value).

e) Detection Limit:

The sensitivity to factors II, V, VII and X of the microINR® System was performed by mixing varying amounts of factor II, V, VII and X deficient plasma, pool normal plasma and red blood cells to final factor concentrations between 100% and 0%. These samples were then tested using nine microINR® Meters and three microINR® Chip lots in each factor sensitivity study. The sensitivity of the microINR® System to factors II, V, VII and X was estimated as 28%, 41%, 37% and 45%, respectively.

f) Analytical Specificity:

Endogenous and Exogenous Interferences

Interference limits were established analyzing fresh venous whole blood, obtained from normal subjects and patients on vitamin K antagonist (VKA) therapy, spiked separately with the interferents.

Substance	Concentration
Acetaminophen	Up to 20 mg/dL
Acetazolamide	Up to 60 mg/L
Acetylsalicylic Acid	Up to 83 mg/dL
Atenolol	Up to 10 mg/L
Bilirubin	Up to 40 mg/dL
Citalopram	Up to 0.8 mg/L
Clopidogrel	Up to 24 mg/dL
Daptomycin	Up to 100 µg/mL
Diclofenac	Up to 54 mg/L
Diltiazem	Up to 5.44 mg/L
Hemoglobin	Up to 1000 mg/dL
Losartan	Up to 50 mg/L
Medroxyprogesterone	Up to 0.81 mg/L
Oritavancin	Up to 7 mg/L
Prasugrel	Up to 16 mg/dL
Pravastatin	Up to 0.6 mg/L
Prednisolone	Up to 3 mg/L
Salicylic Acid	Up to 60 mg/dL
Ticagrelor	Up to 1500 ng/mL
Triglycerides	Up to 3270 mg/dL
Venlafaxine	Up to 0.5 mg/L

The use of heparin, LMWH and fondaparinux is excluded in the instructions for use.

The hematocrit range was evaluated for the microINR® System using blood samples from patients. Venous samples for INR determinations using the microINR® System, citrated plasma samples for the central laboratory INR (Instrumentation Laboratory ACL Elite PRO), and the measured venous whole blood hematocrit for each test subject were used in the analysis. Data analysis demonstrated that hematocrit range between 25 – 55% does not significantly affect test results.

g) Assay cut-off:

Not applicable.

9.2. Comparison Studies

a) Method comparison with Laboratory Reference device

Accuracy was evaluated by comparing the INR results of capillary samples measured on the microINR® System against the INR of venous plasma samples measured on Instrumentation Laboratory ACL TOP® 500 laboratory analyzer using HemosIL® RecombiPlasTin 2G recombinant human tissue thromboplastin reagent (reference device). Results of INR values measured on microINR® System fingerstick capillary whole blood samples were compared to the INR measured on ACL TOP® 500 with HemosIL® RecombiPlasTin 2G using venous plasma samples.

microINR® System vs Laboratory Reference device

N	Slope	Intercept	Pearson (r)
260	1.04	0.02	0.978

b) Matrix comparison

Not applicable, as the microINR® System is intended for use with capillary whole blood samples only.

9.3. 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

9.4. Clinical cut-off

Not applicable.

9.5. Expected values/Reference range

A normal range study was conducted on 134 healthy subjects not on anticoagulation therapy across three sites. Capillary whole blood sample testing performed on the subjects not on vitamin K antagonist therapy demonstrated that 95% of the INR results ranged between 0.8–1.2.

10. INSTRUMENT NAME

microINR® Meter.

11. SYSTEM DESCRIPTION

11.1. Modes of Operation

The microINR® System is a closed system, which is intended to be used exclusively with the microINR® Chips manufactured by iLine Microsystems, S.L.

11.2. Software

The user interface of the microINR® Meter guides the user through the test procedure step by step. The user only needs to insert the Chip and apply a blood sample. The microINR® System measures International Normalized Ratio (INR)

based on a Prothrombin Time (PT) assay and displays the result. After the test is completed, the meter automatically saves the test result.

11.3. 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.

11.4. 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 any risk of human error.

11.5. Quality Control

The microINR® System provides both 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. 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.

In addition to the microINR® On-Board Controls, the microINR® Control has been developed as an optional liquid quality control solution. The microINR® Control must be used only by healthcare professionals in order to meet the regulatory compliance requirements applicable to the facility where they are to be used. The microINR® Control contains lyophilized human citrated plasma from healthy donors (not heparinized plasma or plasma samples under oral anticoagulant therapy) modified by means of a dedicated process to simulate an abnormal coagulation sample and a calcium chloride solution. The microINR® Control assigned acceptable range is included in the Instructions for Use contained in the product box.

12. CONCLUSION

The results of these studies demonstrate that the microINR® System is similar to the predicate in Intended Use. The data presented are a summary of external clinical evaluation, internal laboratory evaluation, and software development information. The microINR® System performance was shown to be substantially equivalent to the predicate device and demonstrated a strong correlation to the reference method.