June 17, 2024

Roche Diagnostics
Amy Pierce
Regulatory Affairs Project Manager
9115 Hague Rd.
P.O. Box 50416
Indianapolis, Indiana 46250

Re: K233060
Trade/Device Name: Elecys Folate III
Regulation Number: 21 CFR 862.1295
Regulation Name: Folic Acid Test System
Regulatory Class: Class II
Product Code: CGN
Dated: May 2, 2024
Received: May 2, 2024

Dear Amy Pierce:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Paula V. Caposino -S

Paula Caposino, Ph.D.
Deputy Division Director
Division of Chemistry and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K233060

Device Name
Elecsys Folate III

Indications for Use *(Describe)*
Binding assay for the in vitro quantitative determination of folate in erythrocytes (red blood cells, RBC). Folate measurements are used in the diagnosis and treatment of anemia. The electrochemiluminescence immunoassay "ECLIA" is intended for use on cobas e immunoassay analyzers.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

Elecsys Folate III
510(k) Summary- K233060

Submitter Name	Roche Diagnostics
Address	9115 Hague Road P.O. Box 50416 Indianapolis, IN 46250-0457
Contact	Amy Pierce Phone: 317-440-5108 Email: amy.pierce.ap2@roche.com
Date Prepared	June 14, 2024
Proprietary Name	Elecsys Folate III
Common Name	Folic acid test system
Classification Name	Acid, Folic, Radioimmunoassay
Product Codes, Regulation Numbers	CGN, 21 CFR 862.1295
Predicate Devices	Roche Diagnostics Elecsys Folate RBC (K103716)
Establishment Registration	Roche Diagnostics GmbH Mannheim, Germany: 9610126 Roche Diagnostics GmBH Penzberg, Germany: 9610529 Roche Diagnostics Indianapolis, IN United States: 1823260

1. DEVICE DESCRIPTION

Elecsys Folate III is a binding assay that makes use of a competitive test principle using a ruthenium labeled folate-binding assay.

Elecsys Folate III is a binding assay for the in vitro quantitative determination of folate in erythrocytes (red blood cells, RBC). Folate measurements are used in the diagnosis and treatment of anemia. The electrochemiluminescence immunoassay “ECLIA” is intended for use on cobas e immunoassay analyzers.

Whole blood treated with anticoagulants (heparin or EDTA) is mixed with ascorbic acid solution and incubated for approximately 90 minutes at 20-25 °C. Lysis of the erythrocytes takes place, with liberation and stabilization of the intracellular folate. The resulting hemolysate sample is then used for subsequent measurement.

Results are determined via a calibration curve, which is instrument-specifically generated by 2-point calibration, and a master curve provided via the cobas link.

1.1. Reagents

The reagent working solutions include cobas e pack (kit placed on the analyzer).

- PT1 Pretreatment reagent 1
- PT2 Pretreatment reagent 2
- M Streptavidin-coated microparticles,
- R1 Folate-binding protein~Ru(bpy)
- R2 Folate~biotin, bis-tris propane buffer

2. INDICATIONS FOR USE

The following Indication for Use is for the Elecsys Folate III

Binding assay for the in vitro quantitative determination of folate in erythrocytes (red blood cells, RBC). Folate measurements are used in the diagnosis and treatment of anemia. The

electrochemiluminescence immunoassay “ECLIA” is intended for use on cobas e immunoassay analyzers.

3. TECHNOLOGICAL CHARACTERISTICS

The table below compares the Elecsys Folate III with its predicate device, Roche Elecsys Folate RBC (K103716).

Item	Elecsys Folate RBC (predicate device)	Elecsys Folate III (candidate device)
Intended Use	This assay is used for the in vitro quantitative determination of folate in erythrocytes (red blood cells, RBC). The electrochemiluminescence binding assay is intended for use on Elecsys and cobas e immunoassay analyzers.	Binding assay for the in vitro quantitative determination of folate in erythrocytes (red blood cells, RBC). Folate measurements are used in the diagnosis and treatment of anemia. The electrochemiluminescence immunoassay “ECLIA” is intended for use on cobas e immunoassay analyzers.
Assay Method	Competitive	No change
Test type	Quantitative	No change
Application time	27 min	No change
Handling of R1 and R2	Liquid, ready to use	No change
Measuring range	120-620 ng/mL	No change
Biotin tolerance	≤ 21 ng/mL	≤ 1200 ng/mL
Sample Anticoagulants	Whole blood treated with anticoagulants Na-heparin or K_3-EDTA	No change
Calibration Interval	Calibration frequency: Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer). Calibration interval may be extended based on acceptable verification of calibration by the laboratory. Renewed calibration is recommended as follows: ▪ after 1 month (28 days) when using the same reagent lot ▪ after 7 days (when using the same reagent kit on the analyzer) ▪ as required: e.g. quality control findings outside the defined limits	Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the cobas e pack was registered on the analyzer). Calibration interval may be extended based on acceptable verification of calibration by the laboratory. Renewed calibration is recommended as follows: ▪ after 12 weeks when using the same reagent lot ▪ after 28 days when using the same cobas e pack on the analyzer ▪ as required: e.g. quality control findings outside the defined limits
Controls	Commercially available whole blood control	No change

Item	Elecsys Folate RBC (predicate device)	Elecsys Folate III (candidate device)
Traceability/Standardization	This application has been standardized against the Elecsys Folate III assay (04476433190)/RBC application. The standardization of the folate RBC application includes the volume correction to account for the preparation of hemolysate sample (1:31 vol/vol).	No change
Reagent Stability	unopened at 2-8 °C: up to the stated expiration date after opening at 2-8 °C: 12 weeks on analyzers: 2 weeks	unopened at 2-8 °C: up to the stated expiration date on analyzers: 2 weeks
Bilirubin tolerance	< 33 mg/dL	≤ 29 mg/dL
Commonly used pharmaceuticals	16	17

4. NON-CLINICAL PERFORMANCE EVALUATION

The following performance data are provided in support of the substantial equivalence determination. All performance specifications were met.

4.1. Precision

4.1.1. Repeatability and Intermediate Precision

Precision measurements were conducted for the updated Elecsys Folate III to evaluate repeatability (within-run precision) and the intermediate precision (within-laboratory precision) according the CLSI guideline EP05-A3. All predefined acceptance criteria was met for the precision experiments.

cobas e 801 analyzer					
		Repeatability		Intermediate precision	
Sample	Mean ng/mL	SD ng/mL	CV %	SD ng/mL	CV %
Hemolysate 1	152	5.73	3.8	6.17	4.1
Hemolysate 2	206	6.14	3.0	7.17	3.5
Hemolysate 3	252	6.70	2.7	8.28	3.3
Hemolysate 4	363	8.01	2.2	10.0	2.8

cobas e 801 analyzer					
		Repeatability		Intermediate precision	
Sample	Mean ng/mL	SD ng/mL	CV %	SD ng/mL	CV %
Hemolysate 5	605	10.7	1.8	14.6	2.4

4.1.2. Lot-to-lot Reproducibility

Precision measurements were conducted according to CLSI guideline EP05-A3 to evaluate Lot-to-Lot Reproducibility using three reagent lots. All predefined acceptance criteria was met for the lot-to-lot reproducibility experiment.

4.2. Analytical Sensitivity

The Limit of Blank (LoB) was determined according to CLSI EP17-A2. The LoB claim in the labeling will be set to 45 ng/mL.

The Limit of Detection (LoD) was determined according to CLSI EP17-A2. The LoD claim in the labeling will be set to 70 ng/mL.

The Limit of Quantitation (LoQ) was determined according to CLSI EP17-A2. The LoQ claim in the labeling will be set to 120 ng/mL.

4.3. Linearity and Dilution

4.3.1. Linearity

Linearity was assessed according to CLSI EP06-Ed2, study design B, using weighted linear regression analysis. At least seven concentrations using hemolysate samples were measured on the **cobas e** 801 analyzer to demonstrate that measurements across the claimed measuring range are linear. Linearity was confirmed to support the measuring range of 120 – 620 ng/mL.

4.3.2. Dilution

A dilution study was performed by using high concentration hemolysate samples that were diluted 1:2 using a 0.2% ascorbic acid solution. The data support instruction for use.

4.4. Endogenous Interferences

The effect of the following endogenous substances were evaluated for potential interference with Elecsys Folate III on the **cobas e** 801 analyzer. All predefined acceptance criteria were met, and the proposed labeling claims for each endogenous substance can be found below:

Compound	Concentration tested
Bilirubin	≤ 29 mg/dL
Intralipid	≤ 1500 mg/dL
Biotin	≤ 1200 ng/mL
Rheumatoid factors	≤ 1000 IU/mL
IgG	≤ 1.6 g/dL
IgA	≤ 0.4 g/dL
IgM	≤ 1 g/dL

4.5. Analytical Specificity/Cross-Reactivity

A cross-reactivity study was conducted with Elecsys Folate III on the **cobas e** 801 analyzer to evaluate the potential cross-reactivity of the assay with the following:

Cross-reactant	Concentration tested ng/mL	Cross-reactivity %
Amethopterin	750	1.7
Aminopterin	750	2.0
Folinic acid	750	2.6

4.6. Exogenous Interferences

An exogenous interference study was conducted to evaluate 17 commonly and 1 specially used pharmaceutical (erythropoietin) compounds for potential interference with the Elecsys Folate III assay on the **cobas e** 801 analyzer. No interference was found.

4.7. Sample Matrix Comparison

The effect on quantitation of analyte in the presence of anticoagulants with Folate III was determined by comparing values obtained from native samples into various tubes containing anticoagulants. Whole blood samples were drawn into Na-Heparin and K_3-EDTA tubes.

The results were within specification and support the use of hemolysate prepared from whole blood and treated with Na-heparin or K_3-EDTA can be used.

4.8. Method Comparison to Predicate

A method comparison was performed using the Elecsys Folate III updated assay and the Elecsys Folate RBC current assay. The results can be found below:

Number of samples measured: 119

Passing/Bablok	Linear regression
$y = 1.04x - 14.6$	$y = 1.03x - 11.0$
$\tau = 0.913$	$r = 0.991$

The sample concentrations were between 132 and 618 ng/mL.

4.9. Reagent Stability

4.9.1. Reagent On-board Stability

On-board reagent stability for the Elecsys Folate III assay was tested on one **cobas e** 801 analyzer. Elecsys Folate III reagent kits can be stored on-board the analyzers for up to 16 weeks.

4.10. Calibration Stability

4.10.1. Lot Calibration Stability

Lot calibration frequency for Elecsys Folate III was tested on one **cobas e** 801 analyzer. Calibration of an Elecsys Folate III reagent lot is recommended every 12 weeks. During that time period, fresh reagent kits of the same lot can be used without calibration using the calibration curve of the day 0 reagent kit.

4.10.2. On-board Calibration Stability

Reagent on-board calibration frequency for Elecsys Folate III was tested on one **cobas e** 801 analyzer. Elecsys Folate III epacks can be stored on board of the analyzers for up to 28 days without a new calibration.

5. EXTERNAL (CLINICAL) TESTING

Not Applicable

6. CLINICAL PERFORMANCE EVALUATION

Not Applicable

7. ADDITIONAL INFORMATION

The Elecsys Folate III is intended to be used with the following calibrators and controls:

- CalSet Folate

CalSet Folate is regulated under product code JIX and 21 CFR 862.1660, is exempt from Premarket notification, and therefore, is not included with this submission.

8. CONCLUSIONS

The information provided in this 510(k) Premarket Notification supports the determination that the updated Elecsys Folate III is substantially equivalent to the predicate device, Elecsys Folate RBC (K103716).