DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

SIEMENS HEALTHCARE DIAGNOSTICS INC.
KIRA GORDON, PHD
SR. REGULATORY AFFAIRS SPECIALIST
511 BENEDICT AVE.
TARRYTOWN NY 10591

August 31, 2017

Re: K171642
Trade/Device Name: Atellica IM Ferritin Assay
Regulation Number: 21 CFR 866.5340
Regulation Name: Ferritin immunological test system
Regulatory Class: II
Product Code: DBF
Dated: May 31, 2017
Received: June 2, 2017

Dear Dr. Gordon:

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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Kelly Oliner -S

For,
Lea Carrington, M.S., MBA, MT
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)*
k171642

Device Name
Atellica IM Ferritin Assay

Indications for Use *(Describe)*
The Atellica™ IM Ferritin (Fer) assay is for in vitro diagnostic use in the quantitative determination of ferritin in human serum and plasma (EDTA and lithium heparin) using the Atellica™ IM Analyzer. This assay can be used as an aid in the diagnosis of iron deficiency anemia and iron overload.

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 of Safety and Effectiveness for the Atellica IM Ferritin Assay

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

1. **510(k) Number:** k171642

2. **Applicant:**

Contact: Kira Gordon, PhD
Sr. Regulatory Affairs Specialist
Address: Siemens Healthcare Diagnostics Inc
511 Benedict Ave,
Tarrytown, NY 10591
Phone: (914) 524-2996
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Email: kira.gordon@siemens-healthineers.com

3. **Date:** August 24, 2017

4. **Proprietary and Established Names:**
Atellica™ IM Ferritin (Fer) Assay

5. **Measureand**
Ferritin

6. **Regulatory Information:**
Atellica™ Ferritin Assay
Classification Names: Ferritin immunological test system.
Regulation Number: 866.5340
Classification: Class II
Product Code: DBF
Trade name: Atellica IM Ferritin Assay
Classification Panel: Immunology

7. **Predicate Devices:**
Device Name: ADVIA Centaur Ferritin Assay
510(k) Number: k992157
Manufacturer: Siemens Healthcare Diagnostics, Inc.

8. **Intended Use:**
See Indications for Use (Section 6)

9. **Indications for Use:**
The Atellica™ IM Ferritin (Fer) assay is for in vitro diagnostic use in the quantitative determination of ferritin in human serum and plasma (EDTA and lithium heparin) using the

Atellica™ IM Analyzer. This assay can be used as an aid in the diagnosis of iron deficiency anemia and iron overload.
Special Conditions for Use Statement(s): For prescription use only

10. **Device Description:**
The Atellica Ferritin Assay kit includes the following components:
Lite Reagent: 5.0 mL/reagent pack. Contains Goat polyclonal anti-ferritin antibody (~0.64 µg/mL) labeled with acridinium ester in HEPES buffer; protein stabilizers; sodium azide (< 0.1%); preservatives
Solid Phase Reagent: 22.5 mL/reagent pack. Contains Mouse monoclonal anti-ferritin antibody (~32.2 µg/mL) covalently coupled to paramagnetic particles in sodium barbital buffer; protein stabilizers; sodium azide (< 0.1%); preservatives

11. Test Principle
Sandwich immunoassay using direct chemiluminometric technology

12. Substantial Equivalence Information:
Device Name: ADVIA Centaur Ferritin Assay
510(k) Number: k992157/k041133
Comparison with Predicate:

Item	**New Device:**	**Predicate Device:**
Intended Use	The Atellica™ IM Ferritin (Fer) assay is for *in vitro* diagnostic use in the quantitative determination of ferritin in human serum and plasma (EDTA and lithium heparin) using the Atellica™ IM Analyzer. This assay can be used as an aid in the diagnosis of iron deficiency anemia and iron overload.	For *in vitro* diagnostic use in the quantitative determination of ferritin in serum or plasma using the ADVIA Centaur®, ADVIA Centaur XP, and ADVIA Centaur XPT systems to aid in the diagnosis of iron deficiency anemia and iron overload.
Instrument	Atellica IM	ADVIA Centaur
Measurement	Quantitative	Same
Technology	Chemiluminescence	Same
Assay Protocol	2-site sandwich immunoassay	Same
Reagents	Lite Reagent - goat polyclonal anti-ferritin antibody labeled with acridinium ester. Solid Phase Reagent - mouse monoclonal anti-ferritin antibody covalently coupled to paramagnetic particles.	Same
Sample type	Serum, Heparinized Plasma, EDTA Plasma	Same
Assay Range	0.9–1650 ng/mL	0.5–1650 ng/mL
Calibrators	2-point calibration	Same

13. Standard/Guidance Document Reference

The following recognized standard and guidance documents were used:

- Format for Traditional and Abbreviated 510(k)s - Guidance for Industry and FDA Staff
- In Vitro Diagnostic Devices: Guidance for the Preparation of 510(k) Submissions
- Guidance for Industry and FDA Staff - Assayed and Unassayed Quality Control Material
- EP05-A3 (7-251) Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline
- EP06-A (7-193) Evaluation of the Linearity Of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- EP07-A2 (7-127) Interference Testing in Clinical Chemistry; Approved Guideline; Approved Guideline
- EP09-A3 (7-245) Measurement Procedure Comparison And Bias Estimation Using Patient Samples; Approved Guideline
- EP17-A2 (7-233) Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline
- EP25-A (7-235) Evaluation of Stability of *In Vitro* Diagnostic Reagents; Approved Guideline
- EP28-A3c (7-224) Defining, Establishing, And Verifying Reference Intervals In The Clinical Laboratory; Approved Guideline

14. Performance Characteristics

Substantial equivalence was demonstrated by testing performance characteristics, listed below, including method comparison, precision, interfering and cross-reactive substances.

1. Analytical Performance

a. Precision

Precision estimates were computed according to CLSI document EP05-A3, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline. Within run (repeatibility) and total imprecision were evaluated by testing 6 serum based samples, calibrators and controls. The elevated levels were spiked with ferritin (liver source) to achieve appropriate concentrations. The samples were assayed in duplicate over the course of 20 days, two runs per day, for a total of 40 runs and 80 replicates.

			Repeatability		Within-Lab	
Sample	Reps	Mean (ng/mL)	SD (ng/mL)	CV (%)	SD (ng/mL)	CV (%)
Serum A	80	4.2	0.15	3.5	0.31	7.2
Serum B	80	8.2	0.14	1.8	0.44	5.4
Serum C	80	41.9	0.57	1.4	1.78	4.2
Serum D	80	65.4	0.82	1.3	2.89	4.4
Serum E	80	118.3	1.44	1.2	4.79	4.0
Serum F	80	487.1	8.00	1.6	20.39	4.2
Serum G	80	779.9	20.69	2.7	44.48	5.7
Serum H	80	1453.6	49.51	3.4	91.40	6.3
Control 1	80	51.8	0.84	1.6	2.49	4.8
Control 2	80	132.7	1.61	1.2	6.01	4.5
Control 3	80	374.0	4.97	1.3	20.69	5.5

b. Linearity/assay reportable range:

Linearity studies were conducted according to *CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures*. Eleven samples with ferritin concentrations distributed throughout the assay range were prepared using high and low human serum pools (low <0.5, ng/mL; high pool >1650 ng/mL concentration of ferritin). Samples were tested in triplicates.

	Observed ng/mL (Y)	**Expected ng/mL**	**Predicted ng/mL ($\hat{Y}$)**	**Predicted % Difference $(Y-\hat{Y})/\hat{Y}*100$**
A	0.20	0.2	-0.71	n/a
B	6.05	7.06	5.57	8.65%
C	11.28	13.93	11.84	-4.69%
D	22.22	27.65	24.39	-8.88%
E	46.04	55.11	49.49	-6.96%
F	98.38	110.03	99.68	-1.30%
G	200.39	219.86	200.07	0.16%
H	401.92	439.53	400.84	0.27%
I	810.18	878.86	802.39	0.97%
J	1267.43	1318.2	1203.94	5.27%
K	1757.53	1757.53	1605.50	9.47%
Weighted linear fit:		Y=0.914*X-0.888		

The linearity data supports analytical measuring range of the Atellica Ferritin Assay of 0.9 - 1650 ng/mL. Values below the LoQ are reported as < 0.9 ng/mL.

c. Detection Limit

Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantification (LoQ) of the Atellica Ferritin Assay were determined according to CLSI EP17- A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.

LoB was determined by testing a total of 6 blank samples (human serum based sample pools with no detectable amounts of ferritin) using two reagent lots in 2 replicates, twice a day over a period of 10 days on one system and over a period of 9 days on a second system. LoB was established as the ferritin value corresponding to the 95th rank position. The LoB was determined to be 0.3 ng/mL.

A total of seven low level human serum-based samples were evaluated using two reagent lots for ten days on one instrument and nine days on a second instrument. The LoD, according to the guideline, is the median or mean of the lowest level material in which the 5th percentile equals or exceeds the Limit of Blank. The LoD was determined to be 0.7 ng/mL.

To calculate LoQ (six low human serum samples were tested using two 2 reagent lots in 8 replicates once a day over a period of 5 days on one system and five low human serum samples were tested using two 2 reagent lots in 8 replicates once a day over a period of 5 days on a second system. LoQ for each reagent lot was determined as the analyte concentration corresponding to 20% within lab CV. The LoQ was determined to be 0.9 ng/mL.

d. Interference

<u>Endogenous Interference</u>

Following guidelines recommended by CLSI EP7-A2, two human serum pools (~20 ng/mL and ~200 ng/mL) were spiked with interferent stock solution (hemoglobin up to 900 mg/dL, triglyceride up to 2000 mg/dL or conjugated and un-conjugated bilirubin up to 60 mg/dL normal) or the same amount diluent (control). Testing was complete on one Atellica system testing all samples in replicates of 3. The interferents showed no significant interference (< ± 10% bias from control) up to the concentrations tested.

Hemoglobin (900 mg/dL)
Triglyceride (2000 mg/dL)
Conjugated Bilirubin (60 mg/dL)
Un-conjugated Bilirubin (60 mg/dL)

Exogenous Interference

Following guidelines recommended by CLSI EP7-A2, two human serum pools (~20 ng/mL and ~200 ng/mL) were spiked with interferent stock solution. Testing was complete on one Atellica system testing all samples in replicates of 3. The interferents showed no significant interference (< ± 10% bias from control) up to the concentrations tested.

Heparin 3000 IU/L
N-acetylcysteine 17.6 mM
Acetysalicylic Acid 2.78 mM
Ampicillin 152 uM
Dobesilate 33.3 ug/mL
Ibuprofen 2425 uM
Levodopa 1.3 mM
Metronidazole 701 uM
Rifampicin 78.1 uM
Theophylline 222 uM
Phenylbutazone 650 uM
Valproic Acid 3.5 mM
Methotrexate 2.0 mM
Prednisone 0.5 mM
Ferrous Sulphate 1.0 mM
Ascorbic Acid 176mg/dL

Specificity (Cross-reactivity)

The cross reactivity of human liver Ferritin and human spleen Ferritin was determined by adding stock solution of liver ferritin and spleen ferritin to four specimens with four different endogenous ferritin levels of approximately 50, 120, 430 and 740 ng/mL). All samples were tested replicates of 3. The results are shown in the following table:

Substance	**Substance Test Concentration (ng/mL)**	**Analyte Concentration (ng/mL)**	**Measured Ferritin Concentration (ng/mL)**	**Cross-Reactivity (%)**
Liver Ferritin	285	52.1	380.3	115%
	285	120.5	401.8	99%
	285	433.8	704.1	95%
	285	741.2	1010.3	94%

Spleen Ferritin	225	51.5	282.5	103%
	225	121.0	342.4	98%
	225	421.4	633.3	94%
	225	739.2	944.9	91%

e. Dilution Recovery Study:

Three human serum samples in the range of 1713.9–1750.6 ng/mL of ferritin were diluted 1:2, 1:4, 1:8, and 1:16 with equine-based diluent and assayed for recovery. The recoveries ranged from 89%–100% with a mean of 94%.

f. Spiking Recovery Study:

Varying amounts of ferritin were added to 5 samples with endogenous ferritin levels of 34.0–321.5 ng/mL. The recoveries ranged from 90%–116% with a mean of 104%.

g. High-dose hook effect:

To test for High Dose "Hook Effect" associated with the Ferritin assay, 11 serial dilution samples were prepared from a sample with 100,000 ng/mL ferritin and tested on Atellica system. The assay did not demonstrate a Hook Effect up to 80,000 ng/mL ferritin

h. Traceability and Stability

Traceability

The Atellica IM Ferritin assay is traceable to World Health Organization 2nd International Standard (WHO 80/578). Assigned values for calibrators are traceable to this standardization.

Stability:

Shelf-life studies:

The shelf-life of the Atellica Ferritin reagents is 8 months at 2-8^{o}C. For unopened product, see the expiration date on the reagent carton.

On-board and open-vial studies:

Reagent On-board reagent stability: for opened products, once placed on the system reagents are stable for 28 days.

Reagent Calibration frequency is assigned at 28 days

Sponsor pre-defined acceptance criteria were met in each of these studies.

2. Comparison Studies

a. Method Comparison with predicate device

A total of 126 serum samples with ferritin concentrations across assay measuring interval were tested using the Atellica IM Ferritin assay and the predicate device. Results were analyzed by both linear and Deming Regression. Final calculations were performed with 107 samples (samples outside the range of either assay were not included in final calculations)

Atellica IM Fer (y) vs Centaur FER (x) (Weighted Deming regression):

y = 1.03x – 0.5 ng/mL, r=0.99, sample range 3.4-1641.4 ng/mL

Note - corr. coefficient calculated using linear regression

b. Matrix Comparison

To evaluate anticoagulant effects, paired serum, K_2 EDTA plasma, Lithium Heparin plasma samples were tested on the Atellica IM Ferritin Assay. A total of 56 paired sample sets were tested. To ensure that the concentrations of ferritin were distributed across the measuring

interval of the assay, five high levels samples spiked with stock solution of ferritin and two diluted samples were included.
Results were analyzed by both linear and Deming Regression.
EDTA plasma (y) vs Serum (x) (Deming regression):
y = 0.96x + 1.6 ng/mL, r=0.997. sample range 2.5–1440.7 ng/mL
Lithium heparin (y) vs Serum(x) (Deming regression):
y = 0.95x + 0.1 ng/mL, r=0.998. sample range 2.5–1440.7 ng/mL
Note - corr. coefficient calculated using linear regression

3. Expected Values/Reference Range

The following values for apparently healthy male (age range 15-95 years old) and female (age range 16-94 years old) subjects with normal liver function enzyme tests, bilirubin, and serum iron tests, were established using the Atellica IM Analyzer in accordance with CLSI Document EP28-A3c

Category	N	Median (ng/mL)	95th Percentile Range (ng/mL)
Normal Males	179	58.9	10.5-307.3
Normal Females	275	46.4	7.3-270.7

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.

15. Proposed Labeling:

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

16. Conclusions

Comparative testing of the Atellica® Ferritin Assay is substantially equivalent in principle and performance to the predicate device - ADVIA Centaur Ferritin assay.