January 18, 2024

Siemens HealthCare Diagnostics Inc.
Anthony Calabro
Regulatory Affairs Specialist
500 GBC Drive
Newark, Delaware 19714

Re: K233242
Trade/Device Name: Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2)
Regulation Number: 21 CFR 866.5270
Regulation Name: C-Reactive Protein Immunological Test System
Regulatory Class: Class II
Product Code: NQD
Dated: October 20, 2023
Received: October 20, 2023

Dear Anthony Calabro:

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.
Acting Deputy 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: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K233242

Device Name

Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2)

Indications for Use *(Describe)*

The Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2) assay is for in vitro diagnostic use in the quantitative determination of the concentration of C-Reactive Protein (CRP) in human serum and plasma (lithium heparin, sodium heparin or K2 EDTA) on the Atellica® CH Analyzer.

Measurements from Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2) may be used as an aid in identification of individuals at risk for future cardiovascular disease. Measurement of hCRP2, when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, may be useful as an independent marker of prognosis for recurrent events in patients with stable coronary disease or acute coronary syndromes.

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.

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510(k) Summary of Safety and Effectiveness

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of 21 CFR 807.92 and the Safe Medical Device Act of 1990.

The assigned 510(k) Number is: K233242

1. Date Prepared

January 18, 2024

2. Applicant Information

Contact: Anthony Calabro
Regulatory Affairs Specialist

Address: Siemens Healthcare Diagnostics Inc
500 GBC Drive
Newark, DE 19714

Email: anthony_calabro@siemens-healthineers.com

3. Regulatory Information

Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2) assay

Trade Name: Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2)
Common Name: Cardiac C-Reactive Protein, Antigen, Antiserum, and Control
Classification Name: C-reactive protein immunological test system
FDA Classification: Class II
Review Panel: Immunology
Product Code: NQD
Regulation Number: 21 CFR 866.5270

4. Predicate Device Information

Predicate Device Name: BN ProSpec System CardioPhase hsCRP
510(k) Number: K212559

510(k) Summary of Safety and Effectiveness

5. Intended Use / Indications For Use

The Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2) assay is for *in vitro* diagnostic use in the quantitative determination of the concentration of C-Reactive Protein (CRP) in human serum and plasma (lithium heparin, sodium heparin or K2 EDTA) on the Atellica® CH Analyzer.

Measurements from Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2) may be used as an aid in identification of individuals at risk for future cardiovascular disease. Measurement of hCRP2, when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, may be useful as an independent marker of prognosis for recurrent events in patients with stable coronary disease or acute coronary syndromes.

Special Conditions for Use Statement: For Prescription Use Only

6. Device Description

The Atellica CH High Sensitivity C-Reactive Protein 2 (hCRP2) assay is used for the quantitative determination of C-Reactive protein in human serum and plasma using the Atellica CH analyzer. This device is two ready-to-use reagent packs consisting of 23.1mL Phosphate buffer, polidocanol (1.9g/L), and sodium azide (0.1%) in Pack 1 and 12.3mL Mouse anti-CRP monoclonal antibodies (13mg/L), polystyrene particles (1g/L), human albumin (0.05%) and sodium azide (<0.1%) in Pack 2. This product consists of two (2) kits consisting of 360 tests each for a total of 720 tests.

Polystyrene particles coated with monoclonal antibodies specific to human CRP are aggregated when mixed with samples containing CRP. These aggregates scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the respective protein in the sample. The result is evaluated by comparison with a standard of known concentration.

The system automatically performs the following steps:
1. For serum/plasma, dispenses 30 µL of primary sample and 90 µL of Atellica CH Diluent into a dilution cuvette.
2. Dispenses 100 µL of Reagent 1 into a reaction cuvette.
3. Dispenses 3 µL of pre-diluted sample into a reaction cuvette.
4. Dispenses 45 µL of Reagent 2 into a reaction cuvette.
5. Mixes and incubates the mixture at 37°C.
6. Measures the absorbance after Reagent 2 addition.
7. Reports results.

Atellica CH High-Sensitivity C-Reactive Protein 2 (hCRP2) assay is used in conjunction with the Atellica CH Analyzer and Atellica CH Protein 2 Calibrator (PROT2 CAL)

510(k) Summary of Safety and Effectiveness

7. Purpose of Submission

The purpose of this submission is a premarket notification for a new device:
Atellica CH High Sensitivity C-Reactive Protein 2 (hCRP2) assay.

8. Comparison of Candidate Device and Predicate Device

The table below describes the similarities and differences between the Atellica CH High Sensitivity C-Reactive Protein 2 assay (Candidate Device) and the BN ProSpec CardioPhase hsCRP (Predicate Device).

Substantial equivalence was demonstrated by testing several performance characteristics including measuring interval, expected values, reference interval, precision, method comparison, interference, and specimen equivalence by method comparison.

510(k) Summary of Safety and Effectiveness

Feature	Candidate Device	Predicate Device
	Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2)	**BN ProSpec CardioPhase hsCRP**
Intended Use	The Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2) assay is for *in vitro* diagnostic use in the quantitative determination of the concentration of C-Reactive Protein (CRP) in human serum and plasma (lithium heparin, sodium heparin or K2 EDTA) on the Atellica® CH Analyzer. Measurements from Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2) may be used as an aid in identification of individuals at risk for future cardiovascular disease. Measurement of hCRP2, when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, may be useful as an independent marker of prognosis for recurrent events in patients with stable coronary disease or acute coronary syndromes.	***Cardio***Phase® ***hs***CRP is an *in-vitro* diagnostic reagent for the quantitative determination of C-reactive protein (CRP) in human serum, and heparin and EDTA plasma by means of particle enhanced immunonephelometry using the BN II and BN ProSpec® System. In acute phase response, increased levels of a number of plasma proteins, including C-reactive protein, is observed. Measurement of CRP is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases*. High sensitivity CRP (hsCRP) measurements may be used as an independent risk marker for the identification of individuals at risk for future cardiovascular disease. Measurements of hsCRP, when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, may be useful as an independent marker of prognosis for recurrent events, in patients with stable coronary disease or acute coronary syndromes.
Sample Type	Human serum and plasma (lithium heparin, sodium heparin, K2 EDTA)	Human Serum, and heparin and K2 EDTA plasma
Units of Measure	mg/L	Same
Assay Range / Measuring Interval	0.16-9.50 mg/L	0.155 – 9.95 mg/L (calibrator lot dependent)
Expected Values	Risk for cardiovascular disease prediction: < 1.00 mg/L are low risk 1.00 mg/L and 3.00 mg/L are average risk > 3.00 mg/L are high risk	Same

510(k) Summary of Safety and Effectiveness

Feature	Candidate Device	Predicate Device
	Atellica® CH High Sensitivity C-Reactive Protein 2 (hCRP2)	**BN ProSpec CardioPhase hsCRP**
Assay Principle	Particle enhanced immunonephelometry	Same
Standardization	ERM-DA474/IFCC	Same
Calibration	Multi-Level calibration	Same
Calibrators	Atellica CH Protein 2 Calibrator (PROT2 CAL)	N Rheumatology Standard SL
Reagents	Two liquid reagents, ready to use	Same
Composition	Pack 1: 23.1 mL Phosphate buffer; polidocanol (1.9 g/L); sodium azide (0.1%) Pack 2: 12.3 mL Mouse anti-CRP monoclonal antibodies (13 mg/L); polystyrene particles (1 g/L); human albumin (0.05%); sodium azide (<0.1%)	Same
Interferences	**Bilirubin, Conjugated**: No Interference ≤ 0.4g/L **Bilirubin, Unconjugated:** No Interference ≤ 0.4g/L **Lipemia:** No Interference ≤ 30g/L **Hemoglobin:** No Interference ≤ 10g/L	**Bilirubin:** No Interference ≤ 0.6g/L **Triglycerides:** No Interference ≤ 16g/L **Hemoglobin:** No Interference ≤ 10g/L

9. Standard/Guidance Document References

510(k) Summary of Safety and Effectiveness

The following recognized standards from Clinical Laboratory Standards Institute (CLSI) were used as a basis of the study procedures described in this submission:

• Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline–Third Edition. (CLSI EP05-A3).
• Interference Testing in Clinical Chemistry (CLSI EP07-ED3).
• Measurement Procedure Comparison and Bias Estimation Using Patient Samples (CLSIEP09c-ED3).
• Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline–Second Edition (EP17-A2).
• Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline (CLSI EP25-A).
• Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition (CLSI EP28-A3c).

The following FDA guidance was followed:

Guidance for Industry and FDA Staff: *Review Criteria for Assessment of C-Reactive Protein (CRP), High Sensitivity C-Reactive Protein (hsCRP) and Cardiac C-Reactive Protein (cCRP) Assays.* Issued on September 22, 2005.

10. Performance Characteristics for Atellica ® CH High Sensitivity C-Reactive Protein 2 (hCRP2)

10.1 Detection Capability

The Limit of Blank (LoB) corresponds to the highest measurement result that is likely to be observed for a blank sample. The assay is designed to have an LoB ≤ Limit of Detection (LoD). LoB was conducted with three (3) reagent lots, six (6) blank samples, and five (5) replicates per sample.

The Limit of Detection (LoD) corresponds to the lowest concentration of c-reactive protein that can be detected with a probability of 95%. The assay is designed to have an LoD ≤ Limit of Quantitation(LoQ). LoD was determined using 495 determinations with 270 blank and 225 low level replicates. Blank samples were 5 lots of Atellica CH diluent and 1 lot of 6% BSA. The 5 low level serum samples were 5 separate human serum samples diluted with Atellica CH diluent targeted to approximately 0.05 mg/L. Three reagent lots were used.

The Limit of Quantitation (LoQ) corresponds to the lowest concentration of c-reactive protein that met the required analyte level but did not reach 20% deviation The assay is designed to have an LoQ of ≤ 0.16mg/L. LoQ samples were prepared by diluting 5 native low analyte serum samples with Atellica CH diluent (saline) to obtain approximately 0.16mg/L. Five replicates of each sample were measured.

Detection capability was determined in accordance with CLSI Documents EP17-A2.

The following results were obtained:

Specimen Type	Detection Capability	Result mg/L
Serum/Plasma	LoB	0.06
	LoD	0.11
	LoQ	0.16

10.2 Precision

Precision was determined in accordance with CLSI Document EP05-A3. Samples were assayed on the Atellica CH Analyzer in duplicate in 2 runs per day for 20 days. The following results were obtained.

Specimen Type	N		Repeatability		Within-Lab	
		Mean mg/L	SD mg/L	CV (%)	SD mg/L	CV (%)
QC1	80	0.81	0.017	2.1	0.020	2.5
Serum 1	80	1.06	0.015	1.4	0.017	1.6
Serum 2	80	2.55	0.021	0.8	0.048	1.9
Serum 3	80	2.90	0.015	0.5	0.023	0.8
Serum 4	80	4.12	0.030	0.7	0.084	2.0
Serum 5	80	8.74	0.065	0.7	0.110	1.3

10.3 Reproducibility

Reproducibility was determined in accordance with CLSI Document EP05-A3. Samples were assayed with 5 replicates per run for 5 days using 3 instruments/sites and 3 reagent lots. The data was analyzed to calculate the following components of precision: repeatability, between-day, between-lot, between-instrument, and reproducibility (total). The following results were obtained.

ASSAY	SAMPLE	N	Mean	Reproducibility									
				Repeatability		Between Day		Between Lot		Between Instrument		Total Reproducibility	
				SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
			mg/L	mg/L	%	mg/L	%	mg/L	%	mg/L	%	mg/L	%
hCRP2	QC1	225	0.72	0.012	1.6	0.001	0.2	0.005	0.6	0.013	1.8	0.018	2.5
hCRP2	Serum 1	225	1.06	0.017	1.6	0.008	0.8	0.000	0.0	0.014	1.3	0.023	2.2
hCRP2	QC2	225	1.86	0.012	0.6	0.008	0.4	0.007	0.4	0.017	0.9	0.023	1.2
hCRP2	Serum 2	225	2.91	0.023	0.8	0.014	0.5	0.000	0.0	0.016	0.5	0.032	1.1
hCRP2	QC3	225	5.63	0.030	0.5	0.018	0.3	0.026	0.5	0.029	0.5	0.052	0.9
hCRP2	Serum 3	225	3.98	0.021	0.5	0.018	0.4	0.023	0.6	0.030	0.7	0.047	1.2
hCRP2	Serum 4	225	7.12	0.045	0.6	0.031	0.4	0.017	0.2	0.064	0.9	0.086	1.2
hCRP2	Serum 5	225	8.56	0.059	0.7	0.062	0.7	0.002	0.0	0.047	0.5	0.098	1.1

10.4 Assay Comparison

The Atellica CH High Sensitivity C-Reactive Protein 2 assay was designed to have correlation coefficient of ≥ 0.950 and a slope of 1.00 ± 0.05 compared to the BN ProSpec CardioPhase hsCRP assay. The following results were obtained using the weighted Deming regression model in accordance with CLSI EP09c.

Specimen Type	Comparison Assay (x)	Regression Equation	Sample Range (mg/L)	N	r
Serum	BN Prospec CardioPhase hsCRP	y = 0.96 x + 0.03 mg/L	0.26 to 9.41	100	0.999

10.5 Specimen Equivalency

The specimen equivalency was determined using the Deming regression model in accordance with CLSI Document EP90c. The following results were obtained:

Specimen Type	Comparison Assay (x)	Regression Equation	Sample Range (mg/L)	N	r
Sodium Heparin	Serum	y=1.07x - 0.02 mg/L	0.22 to 7.40	55	0.998
Potassium EDTA	Serum	y=0.97x - 0.03 mg/L	0.22 to 7.40	55	0.997
Lithium Heparin	Serum	y=1.07x - 0.03 mg/L	0.22 to 7.40	55	0.998

10.6 Interferences

10.6.1 Hemolysis, Icterus, and Lipemia (HIL)

The Atellica CH High Sensitivity C-Reactive Protein 2 assay is designed to have ≤ 10% interference from hemoglobin, bilirubin, and lipemia. Bias is the difference in the results between the control sample (does not contain the interferent) and the test sample (contains the interferent) expressed in a percentage. Bias > 10% is considered interference. Analyte results should not be corrected based on this bias.

Interference testing was performed in accordance with CLSI Document EP07. The following results were obtained:

Substance	**Substance Concentration Conventional Units (SI Units)(g/L)**	**Analyte Concentration Conventional Units**	**Bias %**
Hemoglobin	1000 mg/dL (10 g/L)	0.94 mg/L	4
	1000 mg/dL (10 g/L)	2.30 mg/L	0
Bilirubin, conjugated	40 mg/dL (684 µmol/L)	1.10 mg/L	-1
	40 mg/dL (684 µmol/L)	2.80 mg/L	-1
Bilirubin unconjugated	40 mg/dL (684 µmol/L)	1.10 mg/L	-1
	40 mg/dL (684 µmol/L)	2.82 mg/L	0
Lipemia (Intralipid©)	3000 mg/dL (30 g/L)	0.90 mg/L	-7
	3000 mg/dL (30 g/L)	2.48 mg/L	-4

10.6.2 Non-interfering Substances

The following substances do not interfere with Atellica CH High Sensitivity C-Reactive Protein 2 assay when present in serum and plasma at the concentrations indicated in the table below. Bias due to these substances is ≤ 10%.

Interference testing was performed in accordance with CLSI Document EP07. The following results were obtained:

Substance	Substance Concentration Conventional Units	Analyte Concentration Conventional Units	Bias %
Rheumatoid factors	500 IU/mL	0.94mg/L	-1
	500 IU/mL	2.81mg/L	0

10.6.3 High-Dose Hook Effect / Antigen Excess

High C-reactive protein levels can cause a paradoxical decrease in signal as a result of the high-dose hook effect. In the Atellica CH hCRP2 assay, C-reactive protein levels as high as 1300.00 mg/L will read > 9.50 mg/L.

11. Clinical Study

Not applicable

11.1 Expected Values

A reference interval for healthy adults was verified in accordance with CLSI Document EP28-A3c.

Group	Specimen Type	Reference Interval mg/L
Low risk for cardiovascular disease prediction	Serum/plasma	< 1.00
Average risk for cardiovascular disease prediction	Serum/plasma	1.00-3.00
High risk for cardiovascular disease prediction	Serum/plasma	> 3.00

Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO 3rd, Criqui M, Fadl YY, Fortmann SP, Hong Y, Myers GL, Rifai N, Smith SC Jr, Taubert K, Tracy RP, Vinicor F; Centers for Disease Control and Prevention; American Heart Association. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003 Jan 28;107(3):499-511

12. Standardization

The assay is traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) reference material ERM-DA474/IFCC.

13. Clinical Cut-off

Not applicable

14. Conclusion

The results from the performance studies support that the Candidate Device, Atellica CH High Sensitivity C-Reactive Protein 2 assay is substantially equivalent to the Predicate Device, BN ProSpec CardioPhase hsCRP assay (K212559)