November 8, 2019

Sentinel CH, Spa
Patricia Dupe
Head of Quality System
Via Robert Koch, 2
Milano, 20152 It

Re: K192118
Trade/Device Name: CRP Vario
Regulation Number: 21 CFR 866.5270
Regulation Name: C-Reactive Protein Immunological Test System
Regulatory Class: Class II
Product Code: DCK
Dated: August 1, 2019
Received: August 6, 2019

Dear Patricia Dupe:

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/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 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 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,

Douglas Jeffery, Ph.D.
Chief
Division of Immunology
and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K192118

Device Name
CRP Vario

Indications for Use *(Describe)*
CRP Vario
The CRP Vario assay [CRPVa] is for in vitro diagnostic use in the quantitative immunoturbidimetric determination of C-reactive protein in human serum and plasma (sodium and lithium heparin) using the ARCHITECT c Systems. Measurement of C-reactive protein is useful in the detection and evaluation of infection, tissue injury and inflammatory disorders.

CRP Calibrators (including CRP Calibrator Set, CRP Calibrator HS and CRP Calibrator WR):
CRP Calibrators are intended to be used for the calibration of the CRP Vario for the quantitative determination of C-reactive protein in human serum or plasma samples.

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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Section 15: 510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.
In accordance with 21 CFR 807.87, SENTINEL CH. hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification Special 510(k).
The purpose of this Special 510(k) Premarket Notification is to inform FDA of the proposed modifications to the CRP Vario labeling and provide sufficient detail to support a determination of substantial equivalence.
The primary change in the candidate device, CRP Vario, from the predicated device is the modification in the traceability of the assay from CRM 470 to ERM-DA472/IFCC.

Other changes that will also be addressed are the removal of the EDTA as tube type used for the specimen storage and the revision of the stability of the specimen from 3 years to 1 year when stored at -20°C.

Moreover, other changes to the device labeling implemented since the product initially cleared in 2005 were evaluated per the FDA Guidance document “Deciding When to Submit a 510(k)”. Per the guidance document these changes required documentation only, and they did not present any new risks. The labeling changes are listed below:

- revision of the interference data for Bilirubin which was also separated into Conjugated and Unconjugated Bilirubin
- revision of the High Sensitivity method precision

Note: There were no prior submissions for this device for which FDA provided feedback related to the data or information needed to support substantial equivalence.

Submitter Name	SENTINEL CH. SpA
Address	Via Robert Koch,2 Milano (MI) 20152, Italy
Contact	Primary: Patricia Dupé +39 02 345 514 496 +39 02 345 514 64 patriciadupe@sentinel.it
Date prepared	November 08, 2019
Proprietary Name	CRP Vario
Common name	C-Reactive Protein, Antigen, Antiserum, and Control
Classification Name	C-Reactive Protein, Antigen, Antiserum, and Control Device, (21CFR 866.5270, Class 2 device)
Product Code	DCK
Predicate Devices	The candidate device is a modification of the predicate device. The device name, CRP Vario, is unchanged from how it was cleared in 510(k) k050836 on August 8th, 2005 and CLIA categorized on October 1st,2008
Establishment Registration	The Establishment Registration number for SENTINEL CH. SpA is 9681753

1. DEVICE DESCRIPTION

The CRP Vario assay is intended for the quantitative immunoturbidimetric determination of C-reactive protein in human serum and plasma.
It is supplied as a two-reagent kit which contains 2 reagents composed as follow:

Reactive Ingredients	**Concentration**
Reagent 1: Glycine buffer (pH 7.0)	1.28%
Reagent 2: Anti-CRP polyclonal antibodies (rabbit) adsorbed on latex particles	0.2%

Inactive Ingredients:
Reagent 1: contains bovine albumin (≤ 1%) and sodium azide (< 0.1%).
Reagent 2: contains bovine albumin (≤ 0.1%) and sodium azide (<0.1%).

Two different sizes of the product are available:

REF	**6K26-30**	**6K26-41**
Reagent 1	2 x 37 mL	3 x 86 mL
Reagent 2	2 x 37 mL	3 x 86 mL

A description of the CRP Calibrators, cleared under the same 510(k) k050836, are reported below:

1. CRP Calibrator Set

CRP Calibrator Set contains the following calibrator levels and it is prepared by diluting CRP with human serum and stabilized by adding sodium azide (< 0.1%).

The values assigned and the color of the caps corresponding to each level are indicated in the table below.

Contents of Kit	**Short Name**	**Cap Color**	**Concentration mg/dL**	**Concentration mg/L**	**Quantity**
Calibrator	CRP05	White	0.50	5.0	1 x 2 mL
Calibrator	CRP10	Light yellow	1.00	10.0	1 x 2 mL
Calibrator	CRP20	Light green	2.00	20.0	1 x 2 mL
Calibrator	CRP40	Light blue	4.00	40.0	1 x 2 mL
Calibrator	CRP80	Pink	8.00	80.0	1 x 2 mL
Calibrator	CRP160	Magenta	16.00	160.0	1 x 2 mL
Calibrator	CRP320	Brown	32.00	320.0	1 x 2 mL

To convert results from mg/dL to mg/L, multiply by 10.

2. CRP Calibrator HS

CRP Calibrator HS contains the following calibrator level and it is prepared by diluting CRP with human serum and stabilized by adding sodium azide (< 0.1%).

The value assigned and the color of the cap are indicated in the table below.

Contents of Kit	Short Name	Cap Color	Concentration mg/dL	Concentration mg/L	Quantity
Calibrator	CRPHS	yellow	0.25	2.50	1 x 2 mL

To convert results from mg/dL to mg/L, multiply by 10.

3. CRP Calibrator WR

CRP Calibrator WR contains the following calibrator level and it is prepared by diluting CRP with human serum and stabilized by adding sodium azide (< 0.1%).

The value assigned and the color of the cap are indicated in the table below.

Contents of Kit	Short Name	Cap Color	Concentration mg/dL	Concentration mg/L	Quantity
Calibrator	CRPWR	Green	48.00	480.000	1 x 2 mL

To convert results from mg/dL to mg/L, multiply by 10.

2. INDICATIONS FOR USE

The CRP Vario assay [CRPVa] is for in vitro diagnostic use in the quantitative immunoturbidimetric determination of C-reactive protein in human serum and plasma (sodium and lithium heparin) using the ARCHITECT c Systems. Measurement of C-reactive protein is useful in the detection and evaluation of infection, tissue injury and inflammatory disorders.

CRP Calibrators (including CRP Calibrator Set, CRP Calibrator HS and CRP Calibrator WR) are intended to be used for the calibration of the CRP Vario for the quantitative determination of C-reactive protein in human serum or plasma samples.

3. TECHNOLOGICAL CHARACTERISTICS

The primary change in the candidate device, CRP Vario, from the predicated device is the modification in the traceability of the assay from CRM 470 to ERM-DA472/IFCC.

Other changes that will also be addressed are the removal of the EDTA as tube type used for the specimen storage and the revision of the stability of the specimen from 3 years to 1 year when stored at -20°C.

Moreover, other changes to the device labeling implemented since the product initially cleared in 2005 were evaluated per the FDA Guidance document “Deciding When to Submit a 510(k)”. Per the guidance document these changes required documentation only, and they did not present any new risks. The labeling changes are listed below:

- revision of the interference data for Bilirubin which was also separated into Conjugated and Unconjugated Bilirubin
- revision of the High Sensitivity method precision

The following Table 15-1 and Table 15-2 compare the CRP Vario with its predicate device, CRP Vario (k050836).

Table 15-1: Assay Comparison, General Assay Features

<table>
<tr><th>Feature</th><th>Predicate Device CRP Vario (k050836)</th><th>Candidate Device CRP Vario</th></tr>
<tr><td>Reagent Formulation</td><td>Reactive Ingredient Reagent 1: Glycine buffer (pH 7.0) (1.28%)
Reactive Ingredient Reagent 2: Anti-CRP polyclonal antibodies (rabbit) adsorbed on latex particles (0.2%)</td><td>Same</td></tr>
<tr><td>Classification</td><td>Regulation name: C-Reactive Protein, Antigen, Antiserum, and Control Device</td><td>Same</td></tr>
<tr><td>Test principle</td><td>Turbidimetric / Immunoturbidimetric</td><td>Same</td></tr>
<tr><td>Intended Use</td><td>The CRP Vario assay is used for the quantitative immunoturbidimetric determination of C-reactive protein in human serum and plasma with variable assay ranges [CRP16, CRP32, CRP48] using the ARCHITECT c 8000® System, the ARCHITECT c 16000™ System, and the AEROSET System.</td><td>The CRP Vario assay [CRPVa] is for in vitro diagnostic use in the quantitative immunoturbidimetric determination of C-reactive protein in human serum and plasma (sodium and lithium heparin) using the ARCHITECT c Systems. Measurement of C-reactive protein is useful in the detection and evaluation of infection, tissue injury and inflammatory disorders.</td></tr>
<tr><td>Specimen Type</td><td>Human serum, plasma</td><td>Same</td></tr>
<tr><td>Specimen tube type</td><td>• Serum
• Plasma with the following acceptable anticoagulants:lithium heparin (with or without gel barrier), sodium heparin, and EDTA</td><td>• Serum
• Plasma with the following acceptable anticoagulants: lithium heparin (with or without gel barrier) and sodium heparin</td></tr>
<tr><td>Specimen storage</td><td><table><tr><th>Temperature Storage</th><th>Maximum</th></tr><tr><td>20 to 25°C</td><td>15 days</td></tr><tr><td>2 to 8°C</td><td>2 months</td></tr><tr><td>-20°C</td><td>3 years</td></tr></table></td><td><table><tr><th>Temperature Storage</th><th>Maximum</th></tr><tr><td>20 to 25°C</td><td>15 days</td></tr><tr><td>2 to 8°C</td><td>2 months</td></tr><tr><td>-20°C</td><td>1 year</td></tr></table></td></tr>
<tr><td>Standardization of the calibrator</td><td>This method has been standardized against CRM 470</td><td>This method has been standardized against ERM-DA472/IFCC</td></tr>
</table>

Table 15-2: Assay Comparison, Labeled Performance Characteristics

<table>
<tr><th>Feature</th><th>Predicate Device CRP Vario (k050836)</th><th>Candidate Device CRP Vario</th></tr>
<tr><td>Measuring range</td><td>• High Sensitivity Method 0.01 to 16.00 mg/dL (0.1 to 160 mg/L)
• Standard Method 0.02 to 32.00 mg/dL (0.2 to 320 mg/L)
• Wide Range 0.02 to 48.00 mg/dL (0.2 to 480 mg/L)</td><td>Same</td></tr>
<tr><td>Limit of Quantitation</td><td>• High Sensitivity Method 0.01 mg/dL (0.1 mg/L)
• Standard and Wide Range Methods 0.02 mg/dL (0.2 mg/L)</td><td>Same</td></tr>
<tr><td>Reference range</td><td>Serum and plasma: ≤ 5 mg/L (0.5 mg/dL)</td><td>Same</td></tr>
<tr><td>Analytical Specificity</td><td>The CRP Vario test is not affected by the presence of:
• Rheumatoid Factor up to 550 IU/Ml
• conjugated and fetal bilirubin up to 30 mg/dL
• hemoglobin up to 0.5 g/dL
and lipemia (< 5% intra-lipid approximating 1500 mg/dL of triglycerides).</td><td><table><tr><th>Interefering substance</th><th>Interferent Concentration</th></tr><tr><td>Bilirubin, conjugated</td><td>66 mg/dL (1129 µmol/L)</td></tr><tr><td>Bilirubin, cunonjugated</td><td>66 mg/dL (1129 µmol/L)</td></tr><tr><td>Hemoglobin</td><td>500 mg/dL (5 g/L)</td></tr><tr><td>Intralipid</td><td>1,500 mg/dL (15 g/L)</td></tr><tr><td>Rheumatoid Factor</td><td>550 IU/Ml (550 kU/L)</td></tr></table></td></tr>
<tr><td>Precision</td><td>CRP High Sensitivity Method
<table><tr><th></th><th>mean</th><th colspan="2">Within run</th><th colspan="2">Run to run</th><th colspan="2">Total</th></tr><tr><th></th><th>mg/L</th><th>SD</th><th>CV%</th><th>SD</th><th>CV%</th><th>SD</th><th>CV%</th></tr><tr><td>L1</td><td>0.6</td><td>0.013</td><td>2.10</td><td>0.008</td><td>1.36</td><td>0.015</td><td>2.51</td></tr><tr><td>L2</td><td>5.0</td><td>0.05</td><td>1.02</td><td>0.04</td><td>0.70</td><td>0.06</td><td>1.25</td></tr><tr><td>L3</td><td>18.1</td><td>0.06</td><td>0.32</td><td>0.08</td><td>0.42</td><td>0.09</td><td>0.49</td></tr><tr><td>L4</td><td>70.4</td><td>0.26</td><td>0.38</td><td>0.27</td><td>0.38</td><td>0.35</td><td>0.50</td></tr></table>CRP Standard Method
<table><tr><th></th><th>mean</th><th colspan="2">Within run</th><th colspan="2">Run to run</th><th colspan="2">Total</th></tr><tr><th></th><th>mg/L</th><th>SD</th><th>CV%</th><th>SD</th><th>CV%</th><th>SD</th><th>CV%</th></tr><tr><td>L1</td><td>5.1</td><td>0.10</td><td>1.97</td><td>0.04</td><td>0.86</td><td>0.11</td><td>2.15</td></tr><tr><td>L2</td><td>18.3</td><td>0.11</td><td>0.59</td><td>0.12</td><td>0.65</td><td>0.19</td><td>1.04</td></tr><tr><td>L3</td><td>73.3</td><td>0.37</td><td>0.50</td><td>0.14</td><td>0.19</td><td>0.40</td><td>0.54</td></tr></table>CRP Wide Range Method
<table><tr><th></th><th>mean</th><th colspan="2">Within run</th><th colspan="2">Run to run</th><th colspan="2">Total</th></tr><tr><th></th><th>mg/L</th><th>SD</th><th>CV%</th><th>SD</th><th>CV%</th><th>SD</th><th>CV%</th></tr><tr><td>L1</td><td>5.2</td><td>0.06</td><td>1.16</td><td>0.05</td><td>0.98</td><td>0.10</td><td>1.91</td></tr><tr><td>L2</td><td>18.4</td><td>0.18</td><td>0.99</td><td>0.08</td><td>0.44</td><td>0.22</td><td>1.17</td></tr><tr><td>L3</td><td>268.0</td><td>3.32</td><td>1.24</td><td>3.35</td><td>1.25</td><td>4.92</td><td>1.83</td></tr></table></td><td>CRP High Sensitivity Method
<table><tr><th></th><th></th><th>Level 1</th><th>Level 2</th><th>Level 3</th><th>Level 4</th></tr><tr><td>N</td><td></td><td>40</td><td>40</td><td>40</td><td>40</td></tr><tr><td>Mean (mg/L)</td><td></td><td>0.462</td><td>4.92</td><td>11.35</td><td>45.88</td></tr><tr><td>Within Run</td><td>SD</td><td>0.019</td><td>0.035</td><td>0.148</td><td>0.298</td></tr><tr><td></td><td>%CV</td><td>4.00</td><td>0.72</td><td>1.30</td><td>0.65</td></tr><tr><td>Between Run</td><td>SD</td><td>0.011</td><td>0.024</td><td>0.109</td><td>0.120</td></tr><tr><td></td><td>%CV</td><td>2.38</td><td>0.49</td><td>0.96</td><td>0.26</td></tr><tr><td>Total</td><td>SD</td><td>0.022</td><td>0.043</td><td>0.183</td><td>0.389</td></tr><tr><td></td><td>%CV</td><td>4.66</td><td>0.87</td><td>1.62</td><td>0.85</td></tr></table>NOTE: %CV was calculated prior to rounding Mean and SD.
CRP Standard Method
<table><tr><th></th><th></th><th>Level 1</th><th>Level 2</th><th>Level 3</th><th>Level 4</th></tr><tr><td>N</td><td></td><td>40</td><td>40</td><td>40</td><td>40</td></tr><tr><td>Mean (mg/L)</td><td></td><td>5.10</td><td>18.30</td><td>73.30</td><td>319.40</td></tr><tr><td>Within Run</td><td>SD</td><td>0.10</td><td>0.11</td><td>0.37</td><td>2.08</td></tr><tr><td></td><td>%CV</td><td>1.97</td><td>0.59</td><td>0.50</td><td>0.65</td></tr><tr><td>Between Run</td><td>SD</td><td>0.04</td><td>0.12</td><td>0.14</td><td>1.12</td></tr><tr><td></td><td>%CV</td><td>0.78</td><td>0.65</td><td>0.19</td><td>0.35</td></tr><tr><td>Total</td><td>SD</td><td>0.11</td><td>0.19</td><td>0.40</td><td>2.70</td></tr><tr><td></td><td>%CV</td><td>2.15</td><td>1.04</td><td>0.54</td><td>0.85</td></tr></table>NOTE: %CV was calculated prior to rounding Mean and SD.
CRP Wide Range Method
<table><tr><th></th><th></th><th>Level 1</th><th>Level 2</th><th>Level 3</th><th>Level 4</th></tr><tr><td>N</td><td></td><td>40</td><td>40</td><td>40</td><td>40</td></tr><tr><td>Mean (mg/L)</td><td></td><td>5.20</td><td>18.40</td><td>90.20</td><td>268.00</td></tr><tr><td>Within Run</td><td>SD</td><td>0.06</td><td>0.18</td><td>0.69</td><td>3.32</td></tr><tr><td></td><td>%CV</td><td>1.16</td><td>0.99</td><td>0.77</td><td>1.24</td></tr><tr><td>Between Run</td><td>SD</td><td>0.05</td><td>0.08</td><td>0.76</td><td>3.35</td></tr><tr><td></td><td>%CV</td><td>0.98</td><td>0.44</td><td>0.84</td><td>1.25</td></tr><tr><td>Total</td><td>SD</td><td>0.1</td><td>0.22</td><td>1.25</td><td>4.92</td></tr><tr><td></td><td>%CV</td><td>1.91</td><td>1.17</td><td>1.39</td><td>1.83</td></tr></table></td></tr>
</table>

<table>
<tr><th>Feature</th><th>Predicate Device CRP Vario (k050836)</th><th>Candidate Device CRP Vario</th></tr>
<tr><td>Method comparison</td><td>
<table>
<tr><th>CRP High Sensitivity Method</th><th>AEROSET vs. Nephelometer</th><th>ARCHITECT vs. AEROSET</th></tr>
<tr><td>N</td><td>45</td><td>45</td></tr>
<tr><td>Y - Intercept (95% CI*)</td><td>-0.24 to 0.54</td><td>-0.33 to 0.45</td></tr>
<tr><td>Correlation Coefficient</td><td>0.9994</td><td>0.9994</td></tr>
<tr><td>Slope (95% CI*)</td><td>0.985 to 1.006</td><td>0.975 to 0.996</td></tr>
<tr><td>Standard Error of the Estimate</td><td>0.96</td><td>0.96</td></tr>
<tr><td>Range (mg/L)</td><td>1.0 to 104.0</td><td>1.1 to 103.3</td></tr>
</table>
* CI = Confidence Interval
<table>
<tr><th>CRP High Sensitivity Method (continued)</th><th>AEROSET vs. Turbidimetric Method</th><th>ARCHITECT vs. Turbidimetric Method</th></tr>
<tr><td>N</td><td>55</td><td>55</td></tr>
<tr><td>Y - Intercept (95% CI*)</td><td>-0.01 to 0.07</td><td>-0.02 to 0.10</td></tr>
<tr><td>Correlation Coefficient</td><td>0.9995</td><td>0.9990</td></tr>
<tr><td>Slope (95% CI*)</td><td>0.992 to 1.009</td><td>1.001 to 1.035</td></tr>
<tr><td>Standard Error of the Estimate</td><td>0.10</td><td>0.14</td></tr>
<tr><td>Range (mg/L)</td><td>0.2 to 13.6</td><td>0.2 to 13.6</td></tr>
</table>
* CI = Confidence Interval
<table>
<tr><th>CRP Standard Method</th><th>AEROSET vs. Nephelometer</th><th>ARCHITECT vs. AEROSET</th></tr>
<tr><td>N</td><td>54</td><td>54</td></tr>
<tr><td>Y - Intercept (95% CI*)</td><td>-0.68 to 0.50</td><td>-0.64 to 0.46</td></tr>
<tr><td>Correlation Coefficient</td><td>0.9996</td><td>0.9997</td></tr>
<tr><td>Slope (95% CI*)</td><td>1.004 to 1.020</td><td>0.977 to 0.991</td></tr>
<tr><td>Standard Error of the Estimate</td><td>1.64</td><td>1.58</td></tr>
<tr><td>Range (mg/L)</td><td>1.0 to 219.0</td><td>0.6 to 223</td></tr>
</table>
* CI = Confidence Interval
<table>
<tr><th>CRP Wide Range Method</th><th>AEROSET vs. Nephelometer</th><th>ARCHITECT vs. AEROSET</th></tr>
<tr><td>N</td><td>59</td><td>59</td></tr>
<tr><td>Y - Intercept (95% CI*)</td><td>-1.26 to 1.53</td><td>-1.44 to 2.04</td></tr>
<tr><td>Correlation Coefficient</td><td>0.9989</td><td>0.9982</td></tr>
<tr><td>Slope (95% CI*)</td><td>1.023 to 1.051</td><td>0.968 to 0.999</td></tr>
<tr><td>Standard Error of the Estimate</td><td>4.10</td><td>5.28</td></tr>
<tr><td>Range (mg/L)</td><td>1.0 to 286.0</td><td>0.7 to 301.2</td></tr>
</table>
* CI = Confidence Interval
</td><td>Same</td></tr>
<tr><td>Shelf Life</td><td>The shelf life for the CRP Vario is 18 months from date of manufacture.

The shelf life for the CRP Calibrator Set, CRP Calibrator WR and CRP Calibrator HS is 24 months from date of manufacture.</td><td>Same</td></tr>
</table>

4. SUMMARY OF PERFORMANCE EVALUATION

The risk analysis method used to assess the impact of the modifications was a Failure Modes and Effects Analysis (FMEA).
Based on the risk analysis, the modification to the CRP Vario standardization method did not introduce any new risk to the performance of the assay.
To address the modification, verification and validation activities, which are summarized below, demonstrated that all of the acceptance criteria were met.

Linearity

Linearity evaluation followed the recommendations outlined in Clinical and Laboratory Standards Institute (CLSI) document EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: a Statistical Approach: Approved Guideline.

A high CRP serum pool was mixed with different proportions of a low serum pool to generate 12 concentrations with each concentration level tested in triplicate determinations.

Linear results were compared to 2nd and 3rd order polynomial fits against a pre-specified allowable error.

The linearity range was found to extend up to:

- 16.00 mg/dL for the High Sensitivity Method
- 32.00 mg/dL for the Standard Method
- 48.00 mg/dL for the Wide Range Method

Method Comparison

The primary change in the candidate device, CRP Vario, from the predicated device is the modification in the traceability of the assay from CRM 470 to ERM-DA472/IFCC. As this change was introduced in 2010, the Sentinel predicate device, which is the CRP Vario on market, is now traceable to ERM-DA472/IFCC and therefore this predicate device cannot be used for the Method comparison study. As such, the method comparison study has been conducted using Beckman Coulter CRP Latex REF. OSR6199, which is traceable to CRM 470 (cleared under 510(k) k051564) on AU5800 platform (cleared under 510(k) k112412).

The Method Comparison was tested using the recommendations of CLSI Protocol EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples.
Human serum samples, spanning the measuring range, were tested with the candidate CRP Vario assay (traceable to ERM-DA472) on an ARCHITECT c8000 analyzer and compared to the predicate method (Beckman Coulter CRP Latex REF. OSR6199, traceable to CRM 470) on a Beckman AU5800 analyzer. The correlation between the assays for each method is summarized below.

Representative results analyzed using the Passing-Bablok regression method are summarized in Table 15-3 below. Please note that the regression analysis was performed taking the mean value of the predicate method (Beckman) versus the 1st replicate of the candidate method (c8000).

Table 15-3: Results of the Method Comparison between the Candidate Sentinel device CRP Vario (LN. 6K26) and Beckman Coulter CRP Latex (REF. OSR6199).

Method	**Acceptance Criteria**	**Results**
High Sensitivity Method	Slope 0.95 – 1.05 R ≥ 0.975 n ≥ 100	***Mean Beckman vs 1st rep c8000*** Slope 0.969 (0.964 – 0.974) Intercept 0.019 (0.001 – 0.036) mg/dL r 1.000 n 111 range: (0.01 – 15.71) mg/dL
Standard Method	Slope 0.95 – 1.05 R ≥ 0.975 n ≥ 100	***Mean Beckman vs 1st rep c8000*** Slope 0.956 (0.925 – 0.997) Intercept -0.008 (-0.015 – -0.003) mg/dL r 1.000 n 119 range: (0.01 – 27.74) mg/dL
Wide Range Method	Slope 0.95 – 1.05 R ≥ 0.975 n ≥ 100	***Mean Beckman vs 1st rep c8000*** Slope 0.976 (0.944 – 0.993) Intercept -0.012 (-0.022 – -0.007) mg/dL r 1.000 n 119 range: (0.02 – 43.31) mg/dL

Limit of Quantitation

A study was conducted to assess the sensitivity of CRP Vario High Sensitivity (HS), Standard (Std) and Wide Range (WR) methods.
The LoQ study was performed based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP17-A2. The LOQ was determined using low-level analyte samples prepared at target levels concentrations of 0.08, 0.06, 0.05, 0.04, 0.03, 0.02, 0.01, and 0.005 mg/dL by diluting serum pool with SeraSub (a synthetic serum). Testing occurred over a minimum of 3 days, on 1 ARCHITECT c8000 System. Each sample was tested in a minimum of 10 replicates per run with 2 runs per day over 3 days, for a total of 60 replicates per sample.

At a minimum the limit of quantitation shall be ≤ 0.03 mg/dL for hsCRP and ≤ 0.05 mg/dL for standard and Wide Range methods.
The LOQ results are consistent with the original submission.

5. CONCLUSIONS

The differences between predicate and candidate do not impact the indications for use or technological characteristics.

The conclusions drawn from the nonclinical tests (discussed above) demonstrate the modified CRP Vario are as safe and effective as the predicate device.
The information submitted in the premarket notification is complete and supports a substantial equivalence decision.