

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k050836

B. Purpose for Submission:

Clearance of C-Reactive Protein (CRP) under the Sentinel name for use on Abbott's Aeroset and Architect c8000 Systems. Assay reagents, calibrators and controls were previously cleared under k030545, k030546 and k011169 respectively.

C. Measurand:

C-Reactive Protein

D. Type of Test:

Quantitative/ immunoturbidimetry

E. Applicant:

SENTINEL CH. SRL

F. Proprietary and Established Names:

CRP DIAGNOSTIC ASSAY

G. Regulatory Information:

1. Regulation section:
21CFR Sec.- 866.5270-C-reactive protein immunological test system.
862.1150-Calibrator
862.1660-Quality control material (assayed and unassayed)
2. Classification:
Class 2 (Reagent, Calibrator)
Class 1 (Control)
3. Product code:
DCK - C-reactive protein, antigen, antiserum, and control
JIS - Calibrator, primary
JJY - Multi-analyte controls, all kinds (assayed and unassayed)
4. Panel:
Immunology (82) and chemistry (75)

H. Intended Use:

1. Intended use(s):
see indications for use below
2. Indication(s) for use:
CRP Vario is an in vitro diagnostic test for the quantitative determination of C-reactive protein in human serum and lithium heparin or EDTA plasma samples by immunoturbidimetry. Measurement of C-reactive protein is useful in the detection

and evaluation of infection, tissue injury and inflammatory disorders.

CRP Calibrators (CRP Calibrator Set, CRP Calibrator US 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 and EDTA or lithium heparinized plasma samples.

CRP Control US is intended for use as an assayed quality control material for serum C-reactive protein analysis.

3. Special conditions for use statement(s):

The following limitation on the use of the High Sensitivity CRP should be noted:

- Screening the entire adult population is not recommended;
- CRP is not a substitute for traditional cardiovascular risk factors;
- Acute coronary syndrome management should not depend on CRP measurements;
- When being used for risk assessment, patients with persistently unexplained CRP levels above 10 mg/L should be evaluated for other non-cardiovascular origins;
- Testing for any risk assessment should not be performed while there is indication of infection, systemic inflammation, or trauma;
- Secondary prevention measures should be based on global risk assessment and not depend on CRP;
- Serial measurements of CRP should not be used to monitor treatment;
- The average of CRP results repeated optimally two weeks apart should be used in performing risk assessment, on metabolically stable patients.

4. Special instrument requirements:

Abbott Aeroset and Architect c8000 System

I. Device Description:

The CRP Vario kit is a latex in vitro diagnostic immunoassay for the quantitative determination of CRP in human serum and in heparinized and EDTA-plasma.

From the combination of the CRP Vario and the different calibrator kits, each used with specific analyzer settings (each specified as a particular method), three measuring ranges can be achieved. The combination of calibrators, method used and analytical ranges are listed below:

| Application Method | Calibrators | Analytical Range |
|-------------------------|------------------------------------------|------------------|
| Standard Method | CRP Calibrator Set | 0.2 – 320 mg/L |
| High Sensitivity Method | CRP Calibrator Set and CRP Calibrator US | 0.1 – 160 mg/L |
| Wide Range Method | CRP Calibrator Set and CRP Calibrator WR | 0.2 – 480 mg/L |

J. Substantial Equivalence Information:

1. Predicate device name(s):
DENKA SEIKEN, CRP Latex (II)x2 Assay
2. Predicate 510(k) number(s):
k030545
3. Comparison with predicate:

| Analyzer-related parameters | New Device Vario CRP | Predicate Device CRP-Latex (II)X2 SEIKEN |
|-----------------------------------------------------|--------------------------------------------------------------|---------------------------------------------------|
| Analyzer | Abbott AEROSET [®] or Abbott ARCHITECT [®] | Generic Automated Analyzers (example Hitachi 911) |
| Assay code (Reaction type) | Rate up (Kinetic) | 2 point end (Fixed Time) |
| Assay point instrument cycle numbers (Reading time) | 20 - 26 (360 sec – 468 sec) | 18 - 27 (360 sec - 540 sec) |
| Sample volume (in ml) | | |
| High Sensitivity | 4 | 6 |
| Standard | 2 | 3 |
| Wide Range | 2 | n/a |
| R1 volume | | |
| High Sensitivity | 100 | 150 |
| Standard | 100 | 150 |
| Wide Range | 120 | n/a |
| R2 volume | | |
| High Sensitivity | 100 | 150 |
| Standard | 100 | 150 |
| Wide Range | 120 | n/a |
| Ratio: (R1+R2)/Sample | | |
| High Sensitivity | 50 | Same |
| Standard | 100 | Same |
| Wide Range | 120 | n/a |
| Wavelength | 572 nm monochromatism | 800 / 570 nm bichromatism |
| Calibration method | Spline | same |
| Units / results units | mg/dL or mg/L | mg/L |

K. Standard/Guidance Document Referenced (if applicable):

Evaluation of the Linearity of Quantitative Measurement Procedures, A Statistical Approach; Approved Guideline (2003), CLSI/NCCLS, EP6-A

L. Test Principle:

Human CRP antigens in the sample bind to the specific anti-CRP antibody absorbed onto latex particles, and agglutination occurs. This agglutination is detected as an absorbance change when read between 550-580 nm on an automated chemistry analyzer. The magnitude of the change in absorbance is proportional to the quantity of CRP in the sample. The actual concentration is then determined by interpolation from a calibration curve prepared from kit calibrators of known concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

AEROSSET

CRP High Sensitivity Method

| | mean | Within run | | Run to run | | Total | |
|-----------|------|------------|------|------------|------|-------|------|
| | mg/L | SD | CV% | SD | CV% | SD | CV% |
| L1 | 0.6 | 0.022 | 3.62 | 0.005 | 0.85 | 0.022 | 3.72 |
| L2 | 5.0 | 0.070 | 1.32 | 0.020 | 0.38 | 0.070 | 1.46 |
| L3 | 14.9 | 0.130 | 0.86 | 0.100 | 0.64 | 0.160 | 1.04 |
| L4 | 53.0 | 0.260 | 0.50 | 0.330 | 0.62 | 0.400 | 0.76 |

CRP Standard Method

| | mean | Within run | | Run to run | | Total | |
|-----------|------|------------|------|------------|------|-------|------|
| | mg/L | SD | CV% | SD | CV% | SD | CV% |
| L1 | 5.0 | 0.060 | 1.11 | 0.040 | 0.80 | 0.070 | 1.41 |
| L2 | 14.9 | 0.140 | 0.93 | 0.130 | 0.89 | 0.180 | 1.21 |
| L3 | 53.8 | 0.500 | 0.92 | 0.470 | 0.87 | 0.640 | 1.19 |

CRP Wide Range Method

| | mean | Within run | | Run to run | | Total | |
|-----------|-------|------------|------|------------|------|-------|------|
| | mg/L | SD | CV% | SD | CV% | SD | CV% |
| L1 | 5.4 | 0.070 | 1.29 | 0.050 | 0.92 | 0.080 | 1.48 |
| L2 | 18.3 | 0.170 | 0.93 | 0.130 | 0.71 | 0.220 | 1.18 |
| L3 | 263.8 | 2.990 | 1.13 | 2.650 | 1.00 | 4.020 | 1.52 |

ARCHITECT

CRP High Sensitivity Method

| | mean | Within run | | Run to run | | Total | |
|-----------|------|------------|------|------------|------|-------|------|
| | mg/L | SD | CV% | SD | CV% | SD | CV% |
| L1 | 0.6 | 0.013 | 2.10 | 0.008 | 1.36 | 0.015 | 2.51 |

| | | | | | | | |
|-----------|------|-------|------|-------|------|-------|------|
| L2 | 5.0 | 0.050 | 1.02 | 0.040 | 0.70 | 0.060 | 1.25 |
| L3 | 18.1 | 0.060 | 0.32 | 0.080 | 0.42 | 0.090 | 0.49 |
| L4 | 70.4 | 0.260 | 0.38 | 0.270 | 0.38 | 0.350 | 0.50 |

CRP Standard Method

| | mean | Within run | | Run to run | | Total | |
|-----------|------|------------|------|------------|------|-------|------|
| | mg/L | SD | CV% | SD | CV% | SD | CV % |
| L1 | 5.1 | 0.100 | 1.97 | 0.040 | 0.86 | 0.110 | 2.15 |
| L2 | 18.3 | 0.110 | 0.59 | 0.120 | 0.65 | 0.190 | 1.04 |
| L3 | 73.3 | 0.370 | 0.50 | 0.140 | 0.19 | 0.400 | 0.54 |

CRP Wide Range Method

| | mean | Within run | | Run to run | | Total | |
|-----------|-------|------------|------|------------|------|-------|------|
| | mg/L | SD | CV% | SD | CV% | SD | CV% |
| L1 | 5.2 | 0.060 | 1.16 | 0.050 | 0.98 | 0.110 | 1.91 |
| L2 | 18.4 | 0.180 | 0.99 | 0.080 | 0.44 | 0.220 | 1.17 |
| L3 | 268.0 | 3.320 | 1.24 | 3.350 | 1.25 | 4.920 | 1.83 |

b. Linearity/assay reportable range:

Linearity was determined by serial dilution of the Wide Range CRP Calibrator with normal saline on AEROSET, according to NCCLS EP6-A protocols. 12 dilutions were performed starting from 480 mg/L down to 3 mg/L. The dilutions were the following: 100%, 80%, 60%, 50%, 40%, 30%, 20%, 10%, 5%, 2.5%, 1.25%, 0.625%. Five replicates of each dilution were tested on AEROSET using the three methods. Average value of each dilution was calculated. The sponsor's acceptance criteria used for each testing point (level) was 100% recovery \pm 10% (90 – 110%), calculated as percentage of average found/expected. Also, linear regression was performed using the expected value as the independent variable (x) and mean observed values as the dependent variable (y). Slope, intercept (with 95% Confidence Interval), and Pearson (r²) were calculated through the range accepted by recovery. The sponsor's acceptance criteria for linear regression were: slope= 0.95 to 1.05, Pearson (r) \geq 0.9800.

Acceptable linearity was demonstrated as \geq 160 mg/L for the High Sensitivity method, \geq 320 mg/L for the Standard method, and \geq 480 mg/L for the Wide Range method.

High Sensitivity Method:

Dilutions were deemed acceptable up to 192 mg/L. Linear regression was calculated from 3 to 192 mg/L. Linearity found for this method is from 3 to

179 mg/L. The sponsor claims up to 160 mg/L.

Standard Method:

Dilutions were deemed acceptable up to 384 mg/L. Linear regression was calculated from 3 to 384 mg/L. Linearity found for this method is from 3 to 384 mg/L. The sponsor claims up to 320 mg/L.

Wide Range Method:

Dilutions were deemed acceptable up to 480 mg/L. Linear regression was calculated from 3 to 480 mg/L. Linearity found for this method is from 3 to 480 mg/L. The sponsor claims up to 480 mg/L.

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Subject of k030546 and k011169 clearance

- d. *Detection limit:*

The limit of quantitation for the CRP Vario assay on the AEROSSET System is 0.1 mg/L for the High Sensitivity method, 0.2 mg/L for the Standard method and 0.2 mg/L for the Wide Range Method. This was determined by testing 6 levels of material (0.05, 0.1, 0.2, 0.3, 0.4, and 0.5 mg/L) in replicates of 10 on the AEROSSET. The limit of quantitation was defined as the lowest concentration of analyte with imprecision equal to 20 % CV.

- e. *Analytical specificity:*

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).

- f. *Assay cut-off:*
Not Applicable

2. Comparison studies:

- a. *Method comparison with predicate device:*

The AEROSSET CRP Vario methods (y) were compared with a commercially available nephelometric method (x). The results were as follows:

| | High Sensitivity | Standard | Wide Range |
|--------------------------------|------------------|---------------|---------------|
| Y – Intercept (95% CI) (mg/L) | -0.24 – 0.54 | -0.64 – 0.46 | -1.44 – 2.04 |
| Slope (95% CI) | 0.985 – 1.006 | 0.977 – 0.991 | 0.968 – 0.999 |
| Correlation Coefficient (r) | 0.9994 | 0.9997 | 0.9988 |
| Standard Error of the estimate | 0.96 | 1.58 | 5.28 |
| Number of Samples (n) | 45 | 54 | 59 |
| Min – Max tested value | 1.0 – 104.0 | 0.6 – 223.0 | 0.7 – 301.2 |

A correlation using the High Sensitivity method was performed at relevant

CRP concentrations. Sentinel reagents (y) were compared with a commercially available turbidimetric method (x). The results were as follows:

| | AEROSET | ARCHITECT |
|--------------------------------|---------------|---------------|
| Y – Intercept (95% CI) (mg/L) | -0.01 – 0.07 | -0.02 – 0.10 |
| Slope (95% CI) | 0.992 – 1.009 | 1.000 – 1.035 |
| Correlation Coefficient (r) | 0.9995 | 0.9999 |
| Standard Error of the estimate | 0.09 | 0.14 |
| Number of Samples (n) | 55 | 55 |
| Min – Max tested value | 0.2 – 13.6 | 0.2 – 13.6 |

The ARCHITECT c8000 CRP Vario methods (y) were compared with AEROSET (x). The results were as follows:

| | High Sensitivity | Standard | Wide Range |
|--------------------------------|------------------|---------------|---------------|
| Y – Intercept (95% CI) (mg/L) | -0.33 – 0.45 | -0.68 – 0.50 | -1.26 – 1.53 |
| Slope (95% CI) | 0.975 – 0.996 | 1.004 – 1.020 | 1.023 – 1.051 |
| Correlation Coefficient (r) | 0.9994 | 0.9996 | 0.9989 |
| Standard Error of the estimate | 0.96 | 1.64 | 4.10 |
| Number of Samples (n) | 45 | 54 | 59 |
| Min – Max tested value | 1.1 – 103.3 | 1.0 – 219.0 | 1.0 – 286.0 |

- b. *Matrix comparison:*
Subject of k030545
- 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
- 4. Clinical cut-off:
Not Applicable
- 5. Expected values/Reference range:
< 5.0 mg/L (literature)

N. Proposed Labeling:

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

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.