

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

**A. 510(k) Number:**

k040030

**B. Purpose of Submission:**

New device

**C. Analyte:**

C-reactive protein

**D. Type of Test:**

Solid phase immunodiffusion

**E. Applicant:**

BioCheck, Inc.

**F. Proprietary and Established Names:**

Biocheck CRP Rapid Test

**G. Regulatory Information:**

1. Regulation section:  
21 CFR 866.5270, C-reactive protein immunological test system
2. Classification:  
Class II
3. Product Code:  
DCN, System, test, C-reactive protein
4. Panel:  
82 Immunology

**H. Intended Use:**

1. Intended use(s):  
The BioCheck CRP Rapid Test is intended for the qualitative detection of C-reactive protein (CRP) in human serum.
2. Indication(s) for use:  
Measurements of CRP can be useful for the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases.
3. Special condition for use statement(s):  
Prescription use only.
4. Special instrument Requirements:  
None.

**I. Device Description:**

The BioCheck CRP Rapid Test consists of sample cards (solid phase) pre-loaded with gold-conjugated goat anti-CRP antibody and goat anti-human CRP polyclonal antibody immobilized in a strip across the card. A control strip consisting of anti-Ig is also present on the card to indicate a valid assay.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
Biocheck hsCRP ELISA
2. Predicate K number(s):  
k003851
3. Comparison with predicate:

| Similarities                     |   |   |
|----------------------------------|---|---|
| Item                             | Device  | Predicate   |
| Intended Use                     | The BioCheck CRP Rapid Test is intended for the qualitative detection of C-reactive protein (CRP) in human serum. | The BioCheck hsCRP ELISA is intended for the quantitative determination of C-reactive protein (CRP) in human serum. |
| Specimen                         | Serum   | Same  |
| Differences                      |   |   |
| Item                             | Device  | Predicate   |
| Assay Principle                  | Solid phase chromatographic immunoassay   | ELISA   |
| Assay Type                       | Qualitative   | Quantitative  |
| Solid Phase                      | Antibody coated membrane  | Antibody coated microtiter well   |
| Antibody for solid phase coating | Goat anti-human CRP (Total IgG fractions)   | Mouse monoclonal antibody to human CRP  |
| Conjugate                        | Goat anti-human CRP gold conjugate  | Goat anti-CRP HRP conjugate   |
| Assay evaluation                 | < 4.0 mg/mL, ≥ 4.0 mg/mL, qualitative, visual   | CRP concentration, quantitative, A <sub>450</sub>   |
| Standards                        | None  | Six liquid reference standards  |
| Stability                        | 2-30° C, 18 months  | 2-8° C, 1 year  |

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

None provided

**L. Test Principle:**

The BioCheck CRP Rapid Test is a solid phase chromatographic immunoassay. The device contains a membrane coated with goat anti-human CRP IgG. Near the sample loading site is gold-labeled goat anti-human CRP. After sample application, the CRP

in the sample is bound by both antibodies and migrates across the membrane by capillary action. The gold-labeled fraction of the CRP-antibody conjugate forms a pink color where it is captured by a line of goat polyclonal anti-CRP immobilized on the membrane. Upon further migration of the sample, the conjugate encounters an immobilized strip of anti-Ig, and the CRP-gold antibody conjugate forms a pink control line verifying a valid test.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

Five samples each of CRP at 1.0, 2.0, 3.0, 4.0, and 8.0 mg/mL were tested at three sites plus by two in-house technicians, one set of samples per day for five consecutive days. The test demonstrated 100% agreement with the expected results, and 100% reproducibility within and between days and sites

b. *Linearity/assay reportable range:*

Recovery was examined using serum from a pool of healthy donors, spiked to achieve final CRP concentrations of 1.0, 3.0, 4.0, 6.0, and 8.0 mg/mL. The samples were tested in six replicates and demonstrated 100% agreement with expected results.

c. *Traceability (controls, calibrators, or method):*

The standards for value assignment are traceable to CDC's CRP reference material CRM-470. CRP is purchased from a vendor. The vendor determines the concentration by a commercial nephelometry method whose standards were calibrated with CDC's CRP reference material CRM 470.

d. *Detection limit:*

The assay was designed to detect CRP at  $\geq 4$  mg/mL. The limit of detection was verified in testing at multiple concentrations of CRP above, at, and below the cut-off. The cut-off was verified at 4 mg/mL.

e. *Analytical specificity:*

Interference was tested against potentially interfering substances found in blood: bilirubin (10 mg/dL), hemoglobin (200 mg/dL), cholesterol (800 mg/dL), triglyceride (1250 mg/dL), and biotin (200 ng/mL). Samples with CRP concentrations of 1.8 and 3.6 mg/mL were spiked with interferent and were tested in singlicate. No interference was detected based on the demonstration that all tested samples remained negative. Testing of the same samples by an alternative ELISA test demonstrated that the CRP concentration was unchanged by the addition of the above-listed interfering substances.

Additional specificity was demonstrated against 33 drugs and substances that might be found in blood in persons undergoing testing. These were ascorbic acid, atenolol, atropine, caffeine, captopril, chloramphenicol, cinnarizine, cyclophosphamide, cyclosporine, digitonin, digoxin, dopamine, erythromycin, gentistic acid, isoproterenol, isosorbide dinitrate, nifedipine, nystatin, oxazepam, oxytetracycline, propranolol, theophylline, L-thyroxine, urea, uric acid, verapamil. CRP concentrations of 1.8 and 3.6 mg/mL were spiked with 10 mg/mL of each of these and tested in singlicate. No interference was detected based on the demonstration that all samples remained negative. Testing of the same samples by an alternative ELISA test demonstrated that the CRP concentration was unchanged by the addition of the above-listed interfering substances

*f. Assay cut-off:*

The assay was designed to have a single cut-off near the upper limit of normal, based on the average 90<sup>th</sup> percentile of normal CRP in healthy adults, which has been reported as 4.93 mg/mL in the literature. The cut-off value was verified by testing in triplicate samples with CRP values of 3.0, 3.2, 3.4, 3.6, 3.8, 4.0, 4.2, 4.4, 4.6, and 4.8 mg/mL. Samples at 4.0 mg/mL and above were always positive, samples at 3.8 mg/mL were weakly positive 2 of 3 times, and all samples at lower than 3.8 mg/mL were always negative.

2. Comparison studies:

*a. Method comparison with predicate device:*

A total of 420 samples from three different groups of patients (random, known elevated CRP, cardiac patients with diagnosis) were tested using the device and the results were compared to those generated using the quantitative predicate device. If the predicate reported a value  $\geq 4.0$  mg/mL, and the new device was positive, or the predicate reported a value  $< 4.0$  mg/mL and the new device was negative, these were considered to be positive and negative agreement, respectively.

Group 1: Of 209 random patient samples, the following results were obtained:

| BioCheck CRP Rapid Test | BioCheck CRP ELISA Test |               |
|-------------------------|-------------------------|---------------|
|                         | $\geq 4.0$ mg/mL        | $< 4.0$ mg/mL |
| +                       | 69                      | 4             |
| -                       | 2                       | 134           |
| Total                   | 71                      | 138           |

Positive agreement:  $69/73 = 94.5\%$

Negative agreement:  $134/136 = 98.5\%$

Total agreement:  $203/209 = 97.1\%$

Group 2: Of 67 serum samples from cardiac patients, the following results were obtained:

| <b>BioCheck CRP Rapid Test</b> | <b>BioCheck CRP ELISA Test</b> |               |
|--------------------------------|--------------------------------|---------------|
|                                | $\geq 4.0$ mg/mL               | $< 4.0$ mg/mL |
| +                              | 66                             | 0             |
| -                              | 0                              | 1             |
| Total                          | 66                             | 1             |

Positive, negative and total agreements were 100%.

Group 3: Of 145 serum samples from cardiac patients with known diagnoses, the following results were obtained

| <b>BioCheck CRP Rapid Test</b> | <b>BioCheck CRP ELISA Test</b> |               |
|--------------------------------|--------------------------------|---------------|
|                                | $\geq 4.0$ mg/mL               | $< 4.0$ mg/mL |
| +                              | 69                             | 4             |
| -                              | 1                              | 71            |
| Total                          | 70                             | 75            |

Positive agreement:  $69/70 = 98.6\%$

Negative agreement:  $71/75 = 94.7\%$

Total agreement:  $140/145 = 96.6\%$

*b. Matrix comparison:*

Not applicable

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:

Expected value for normal healthy individuals is  $<4$  mg /mL, determined by 90<sup>th</sup> percentile of CRP concentration in apparently healthy people. In a study of 432 healthy Caucasians, the following values were obtained:

n: 432

Mean: 1.6 U/mL

Mean +2SD 8.8 U/mL

Median: 0.9 U/mL

95<sup>th</sup> percentile 4.5 u/mL

**N. Conclusion:**

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