

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

k062981

B. Purpose for Submission:

New submission

C. Measurand:

C-reactive protein

D. Type of Test:

Quantitative fluorescence immunoassay

E. Applicant:

Boditech Diagnostics, Inc.

F. Proprietary and Established Names:

i-Chroma CRP Test

G. Regulatory Information:

1. Regulation section:

21CFR Sec.- 866.5270-C-reactive protein immunological test system.

2. Classification:

Class II

3. Product code:

DCN - System, Test, C-Reactive Protein

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indication(s) for use below

2. Indication(s) for use:

The i-CHROMA CRP Test along with i-CHROMA Reader is an in vitro diagnostic fluorescence immunoassay that measures C-Reactive Protein in whole blood and serum. Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues, infection, and inflammatory disorders.

3. Special conditions for use statement(s):

Prescription use

Not for cardiovascular risk assessment

4. Special instrument requirements:

i-CHROMA Reader

I. Device Description:

The test kit consists of:

- Test Cassette: 25 test strips, coated with murine monoclonal anti-CRP antiserum, and rabbit IgG immobilized on the test and control line of the strip, respectively.
- Detection Buffer: 25 X 150 μ L, contains fluorescence-labeled anti-CRP (mouse monoclonal), anti-rabbit IgG , protein stabilizer, and sodium azide as preservative in PBS.
- ID Chip: lot and test specific calculation chip.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Behring, Inc., RCRP Flex Reagent Cartridge
2. Predicate 510(k) number(s):
k003419
3. Comparison with predicate:

| Comparison to Predicate Device: | | |
|---------------------------------|---|---|
| Item- | RCRP Flex@ reagent cartridge | i-Chroma CRP Test |
| Sample Type | serum and plasma | serum and whole blood |
| Technology | particle enhanced turbidimetric immunoassay (PETIA) | fluorescence sandwich immunoassay |
| Antibody | goat polyclonal | murine monoclonal + Fluorescence mouse monoclonal anti-CRP |
| Detection | Aggregation (turbidimetric) measurement | fluorescence |
| Indications for use | The High Sensitivity C-Reactive Protein (RCRP) Flex reagent cartridge for the Dimension clinical chemistry system is an in vitro diagnostic test intended for the quantitative determination of C-reactive protein in serum and plasma. Measurement of C-reactive protein is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases. | The i-CHROMA CRP test along with i-CHROMA Reader is an in vitro diagnostic fluorescence immunoassay that measures C-Reactive Protein in whole blood and serum. Measurement of C-Reactive Protein aids in evaluation of the amount of injury to body tissues, infection, and inflammatory disorders. |
| Assay range of measurement | 0.5 mg/L – 250.0 mg/L | 1.3 mg/L – 50 mg/L |

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

None referenced

L. Test Principle:

The i-CHROMA CRP Test is based on fluorescence immunoassay technology. The i-CHROMA CRP Test uses a sandwich immuno-detection method, such that by mixing detector buffer with blood specimen in test vial, the fluorescence-labeled detector anti-CRP antibody in buffer binds to CRP antigen in blood specimen. As the sample

mixture is loaded onto the sample well of the test device and migrates the nitrocellulose matrix of test strip by capillary action, the complexes of detector antibody and CRP are captured to anti-CRP sandwich pair antibody that has been immobilized on test strip. Thus the more CRP antigen is in blood specimen, the more complexes are accumulated on test strip. Signal intensity of fluorescence of detector antibody reflects amount of CRP captured and is microprocessed from i-CHROMA Reader to show CRP concentration in blood specimen.

M. Performance Characteristics (if/when applicable):

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

Intra-Assay

The intra-assay variation was determined by replicate measurements (10) of 4 blood samples using 10 cassettes of the same lot on the same day for 3 different lots of kits. The within assay variability is shown below:

| Conc. (mg/L) | AVG | SD | CV |
|--------------|-------|-------|-----|
| 5 | 5.22 | 0.125 | 2.4 |
| 10 | 9.80 | 0.248 | 2.5 |
| 20 | 19.92 | 0.443 | 2.2 |

An additional study was performed at 3 laboratory sites using pools of whole blood and serum that was aliquoted and sent to the sites for testing. These samples were run in 20 replicates within one run by each site. The following results were obtained by each site for the blood and serum samples.

| | Site 1 Blood | Site 1 serum | Site 2 blood | Site 2 Serum | Site 3 Blood | Site 3 Serum |
|--------|--------------|--------------|--------------|--------------|--------------|--------------|
| Mean | 1.39 | 1.34 | 1.245 | 1.225 | 1.25 | 1.31 |
| S.D. | 0.11 | 0.12 | 0.11 | 0.10 | 0.11 | 0.12 |
| C.V. % | 7.87 | 8.86 | 9.20 | 7.89 | 8.80 | 8.90 |
| Mean | 2.98 | 3.05 | 3.10 | 3.03 | 2.96 | 3.04 |
| S.D. | 0.13 | 0.11 | 0.15 | 0.16 | 0.13 | 0.14 |
| C.V. % | 4.52 | 3.75 | 4.97 | 5.15 | 4.41 | 4.57 |
| Mean | 5.32 | 5.41 | 5.35 | 5.01 | 5.52 | 5.58 |
| S.D. | 0.26 | 0.26 | 0.19 | 0.23 | 0.23 | 0.21 |
| C.V. % | 4.86 | 4.79 | 3.61 | 4.53 | 4.17 | 3.70 |
| Mean | 44.74 | 46.2 | 45.35 | 46.23 | 45.26 | 46.33 |
| S.D. | 2.20 | 1.45 | 1.46 | 0.95 | 2.16 | 1.45 |
| C.V. % | 4.91 | 3.15 | 3.21 | 2.06 | 4.78 | 3.12 |

Inter-Assay

The Inter-assay (between-run) / Inter-Lot variation was determined by triplicate measurements of four blood samples in three different days runs with 3 lots of kits. The precision of the inter-assay (between days) variations was evaluated to determine the accuracy of the *i*-Chroma system. The inter-assays precision studies were performed on 5 sequential days, two runs per day, with 10 results at each concentration.

| Conc. (mg/L) | AVG | SD | CV |
|--------------|--------|-------|-----|
| 5 | 5.207 | 0.245 | 4.7 |
| 10 | 10.078 | 0.455 | 4.5 |
| 20 | 20.078 | 1.107 | 5.5 |

An additional study was performed using 3 laboratory sites. Aliquots of patient serum and whole blood were run at each site for 5 days in singlet to evaluate the Inter-Day and Inter-site reproducibility of the assay. The following Table summarizes the day to day and site to site reproducibility from a total of 15 assays.

Each Site

| | | blood | serum | blood | serum | blood | serum | blood | serum |
|--------|--------|-------|-------|-------|-------|-------|-------|-------|-------|
| Site 1 | Mean | 3.10 | 3.00 | 5.06 | 5.04 | 25.24 | 24.20 | 45.88 | 44.72 |
| | S.D. | 0.07 | 0.10 | 0.15 | 0.18 | 0.73 | 1.56 | 1.25 | 0.56 |
| | C.V. % | 2.28 | 3.33 | 3.00 | 3.60 | 2.88 | 6.43 | 2.72 | 1.26 |
| Site 2 | Mean | 3.08 | 3.00 | 4.72 | 5.24 | 25.34 | 25.66 | 44.34 | 46.04 |
| | S.D. | 0.08 | 0.07 | 0.23 | 0.13 | 0.37 | 0.61 | 2.03 | 0.75 |
| | C.V. % | 2.72 | 2.36 | 4.83 | 2.56 | 1.47 | 2.36 | 4.59 | 1.62 |
| Site 3 | Mean | 2.98 | 3.02 | 5.04 | 5.16 | 23.70 | 25.70 | 43.82 | 45.48 |
| | S.D. | 0.08 | 0.08 | 0.13 | 0.26 | 1.79 | 0.66 | 1.69 | 2.18 |
| | C.V. % | 2.81 | 2.77 | 2.66 | 5.05 | 7.55 | 2.58 | 3.85 | 4.80 |

Site results Combined

| | blood | serum | blood | serum | blood | serum | blood | serum |
|--------|-------|-------|-------|-------|-------|-------|-------|-------|
| Mean | 3.05 | 3.01 | 4.94 | 5.15 | 24.76 | 25.19 | 44.68 | 45.41 |
| S.D. | 0.09 | 0.08 | 0.23 | 0.20 | 1.31 | 1.20 | 1.81 | 1.39 |
| C.V. % | 3.00 | 2.66 | 4.64 | 3.95 | 5.28 | 4.77 | 4.04 | 3.05 |

b. Linearity/assay reportable range:

Recovery of the I-Chroma system was determined by serially diluting controls

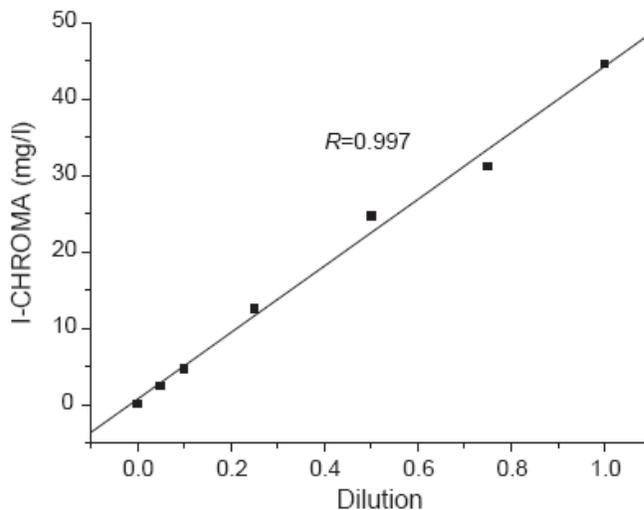
and a sample to 1:32 dilution. Each sample was assayed and recovery of the samples were calculated. The dilution recovery study supports a lower range of measurement of 1.3 mg/L using an acceptance criteria of +/- 10 percent recovery.

| Samples | Dilution | Measurement Value (mg/L) | | | | | |
|-----------------------|----------|--------------------------|-------|-------|-------|-------|-------|
| | | x 1 | x 2 | x 4 | x 8 | x 16 | x 32 |
| Control Serum (High) | Run 1 | 45.2 | 21.0 | 10.2 | 5.4 | 2.4 | 1.4 |
| | Run 2 | 39.8 | 20.7 | 10.5 | 4.8 | 2.6 | 1.5 |
| | Mean | 42.50 | 20.85 | 10.35 | 5.10 | 2.50 | 1.45 |
| Expected Value | | 42.5 | 21.25 | 10.63 | 5.31 | 2.66 | 1.33 |
| Measure/Calculate (%) | | 100 | 98.1 | 97.4 | 96.0 | 94.1 | 109.2 |
| Control Serum (Low) | Run 1 | 4.9 | 2.6 | 1.1 | 0.7 | 0.5 | < 0.5 |
| | Run 2 | 5.3 | 2.3 | 1.3 | 0.8 | 0.5 | < 0.5 |
| | Mean | 5.10 | 2.45 | 1.20 | 0.75 | 0.50 | < 0.5 |
| Expected Value | | 5.1 | 2.55 | 1.28 | 0.64 | 0.32 | 0.16 |
| Measure/Calculate (%) | | 100 | 96.1 | 94.1 | 117.6 | 156.9 | - |

The measurement range of the assay is: 1.3 - 50 mg/L based on the above recovery study and by the below site comparison studies.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The i-CHROMA Reader calculates CRP test results automatically and displays CRP concentration on the screen as mg/L. The test is calibrated against the NIBSC 1st International Standard for human C-Reactive Protein (Code 85/506). The following typical calibration curve was obtained from dilutions of this preparation.



The stability of the I-Chroma kit components was investigated by real-time and accelerated stability studies. To show the reliability of the product, three different Kit-Lots were tested after one to two years storage at 2 - 8°C, RT,

and frozen. The components were found stable for at least 18 months to date when the cassette was stored at temperatures between 2 and 30°C, and the Detector is stored at 2 - 8 °C. Different combinations of refrigerated, frozen, RT, and 37°C were also evaluated. The three lots of I-Chroma kits were examined for real time stability.

Controls are not provided; the manufacturer recommends the use of commercially available controls.

d. Detection limit:

The functional sensitivity (LOQ) of 0.2 mg/L (defined as the concentration at which there was observed % CV < 20) is below the claimed lower limit of the measuring range.

e. Analytical specificity:

To evaluate potential interference, Hemoglobin (1000 mg/dL), Bilirubin (60 mg/dL), or Triglycerides (1600 mg/dL) were added to test specimens ranging from 1.5, 5, and 10 mg CRP/L in blood. The samples were then assayed 10 times with the following results:

| | CRP conc. (mg/l) | Mean | SD | CV (%) |
|----------------------------|------------------|-------|------|--------|
| Hemoglobin (1000 mg/dL) | 1.5 | 1.44 | 0.10 | 7.22 |
| | 5 | 5.04 | 0.41 | 8.11 |
| | 10 | 10.50 | 0.62 | 5.94 |
| Bilirubin (60 mg/dL) | 1.5 | 1.55 | 0.08 | 5.07 |
| | 5 | 4.84 | 0.33 | 6.89 |
| | 10 | 10.21 | 0.61 | 6.01 |
| Triglycerides (1600 mg/dL) | 1.5 | 1.55 | 0.06 | 4.17 |
| | 5 | 5.11 | 0.29 | 5.72 |
| | 10 | 10.27 | 0.61 | 5.95 |

There was no significant interference with the CRP measurement (defined as recovering within +/- 10% of control).

The immunoassay is formulated to help protect from potential interferences with HAMA. Nevertheless, one cannot assure that there will never be a "false positive" result due to the presence of heterophilic antibodies in a patient sample.

f. Assay cut-off:

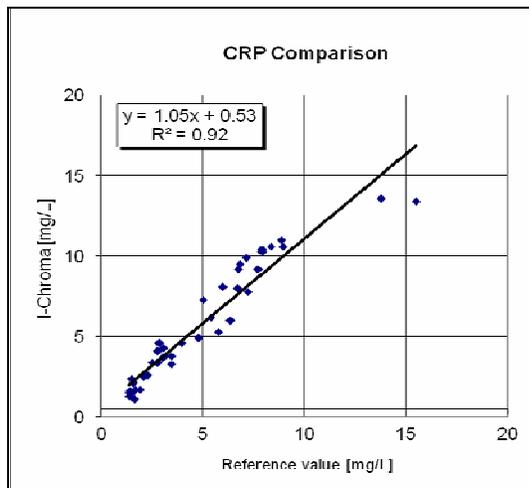
Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

The study compared a commercially available CRP test to the i-Chroma test using 43 whole blood samples randomly collected from 31 - 90 year old subjects visiting clinics and hospital labs for routine testing. No patient information was obtained regarding disease or health conditions. Samples ranging from 1.3 mg/L to 13.6 mg/L were used in the following analysis.

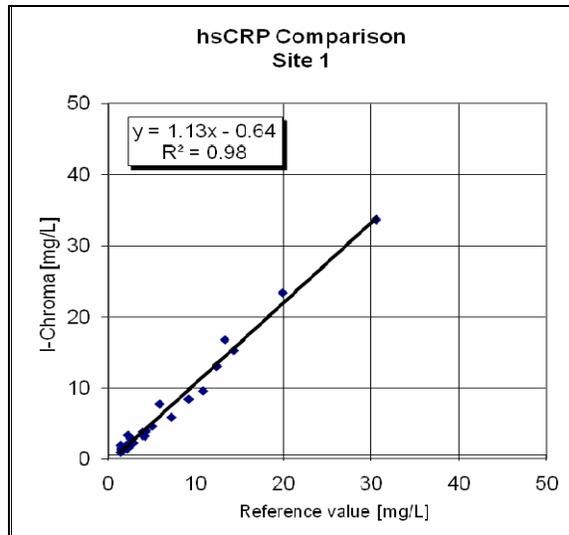
| | |
|------------------|-------|
| R = | 0.958 |
| R ² = | 0.918 |
| Slope = | 1.054 |
| Intercept = | 0.530 |
| N = | 43 |



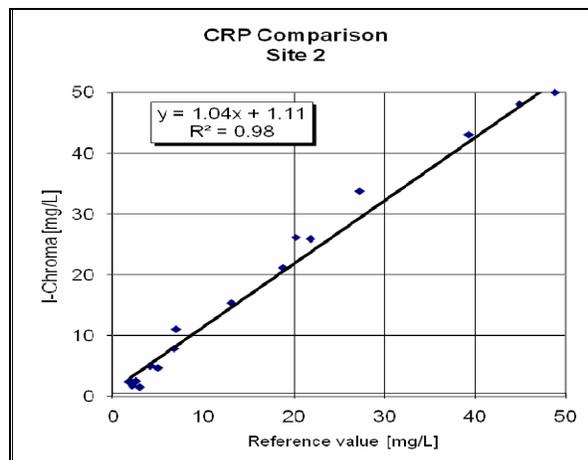
A second comparison study was performed at three sites. Each site was asked to perform a comparative study investigating the relationship between CRP values determined using their reference method for serum, and values determined using i-CHROMA TEST and READER for serum and blood (EDTA) samples. The sites were sent the i-Chroma reader and test cassettes, and the studies at the 3 sites was performed using in-house patient serum and blood samples following manufacturer instructions defined in the insert packages. Each site was asked to obtain blood and serum from patients sent for CRP evaluation by each lab. A total of 99 each of serum and blood samples were evaluated with the following correlation results from samples ranging from 1.3 mg/L to 49.3 mg/L. All samples higher than 50 mg/L by the predicate gave >50 result by i-Chroma.

| Site 1 - Behring | Serum | Blood |
|------------------|-------|-------|
| R = | 0.992 | 0.996 |
| R ² = | 0.985 | 0.991 |

| | | |
|-------------|-------|-------|
| slope = | 1.131 | 1.093 |
| intercept = | -0.64 | -0.45 |
| N = | 34 | 34 |

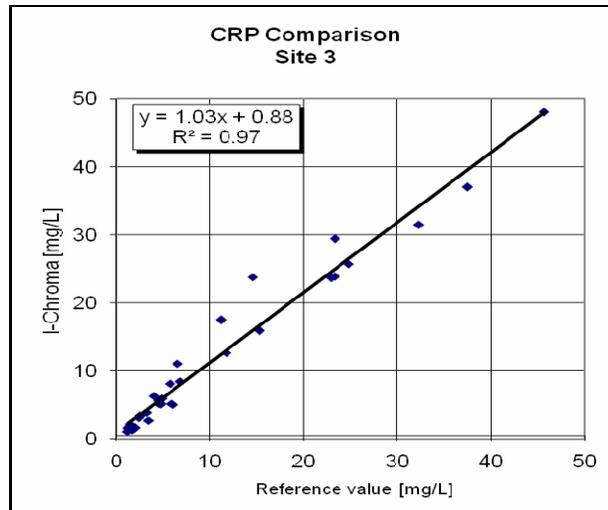


| Site 2 - Fluorescence | Serum | Blood |
|-----------------------|-------|-------|
| R = | 0.992 | 0.974 |
| R sq = | 0.984 | 0.949 |
| Slope = | 1.037 | 0.920 |
| Intercept = | 1.106 | 0.505 |
| n = | 19 | 19 |



| Site 3 – Enhanced Latex | Serum | Blood |
|-------------------------|-------|-------|
| R = | 0.983 | 0.955 |
| R sq = | 0.966 | 0.911 |

| | | |
|-------------|-------|-------|
| Slope = | 1.033 | 1.077 |
| Intercept = | 0.876 | 0.995 |
| n = | 32 | 32 |



- b. *Matrix comparison:*
See method comparison information above
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:

The manufacturer conducted a study using a normal apparently healthy population of 38 adults (males and females) ages 38 to 82 years to assess the CRP range in this normal population using the I-Chroma test. This population demonstrated a mean of 2.38 mg/L with a 2 SD of 3.04 mg/L and 3 SD of 4.55 mg/L. This bridging study is in agreement with published reference ranges for CRP in adult populations.

N. Instrument Name:

i-CHROMA Reader

O. System Descriptions:

The i-CHROMA Reader, manufactured by BodiTech Med Inc., is a portable instrument for fluorescence detection of CRP in serum and whole blood and other analytes in blood and urine that may be adaptable to the reader. The assays and the instrument are for in-vitro diagnostic use only. i-CHROMA Reader uses a laser as the excitation light source. The emitted light from the fluorescence dye is collected and converted into an electrical signal. The signal is related to the amount of fluorescing dye molecules present on the spot under examination.

After a buffer-mixed sample is applied to the Test Device, the Test Device is inserted into i-CHROMA Reader and the concentration of analyte is calculated by a pre-programmed calibration process. i-CHROMA Reader can accept Test Devices that are designed specifically for use with this instrument.

1. Modes of Operation:

Manually or automated (timed) test device (strip cartridge) introduction

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes or No

3. Specimen Identification:

No sample identification data entry

4. Specimen Sampling and Handling:

Single unitized test device (strip cartridge)

5. Calibration:

pre-programmed calibration process

6. Quality Control:

No quality control program

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Q. Proposed Labeling:

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

R. Conclusion:

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