

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

A. 510(k) Number:

k060139

B. Purpose for Submission:

New device

C. Measurand:

C-Reactive Protein

D. Type of Test:

Quantitative immuno-agglutination

E. Applicant:

Diagnostic Chemicals LTD.

F. Proprietary and Established Names:

CRP-ADVANCE ASSAY, MODELS 250-20, 250-25

G. Regulatory Information:

1. Regulation section:
21CFR Sec. - 866.5270-C-reactive protein immunological test system.
2. Classification:
Class 2
3. Product code:
DCK - C-Reactive Protein, Antigen, Antiserum, and Control
4. Panel:
Chemistry (75)

H. Intended Use:

1. Intended use(s):
For the IN VITRO quantitative determination of C-Reactive Protein (CRP) in serum.
2. Indication(s) for use:
For the quantitative determination of C-Reactive Protein (CRP) in serum. For IN VITRO diagnostic use.

A CRP test system is a device intended to measure CRP in serum. C-Reactive Protein (CRP) is an abnormal protein synthesized in the liver during inflammation and necrosis of cellular tissue. This method, using antihuman CRP mouse

antibody coated latex to bind CRP, allows for accurate measurement over a wide range of CRP concentrations. The resulting agglutination from binding is measured spectrophotometrically and is proportional to the concentration of CRP in the sample.

3. Special conditions for use statement(s):
For prescription use
4. Special instrument requirements:
Hitachi 911

I. Device Description:

CRP-ADVANCE Buffer Solution (R1): A solution containing a buffer at pH 8.5.

CRP-ADVANCE Latex Reagent (R2): A solution containing antihuman CRP mouse monoclonal antibody-coated latex (2 mg/dL).

DCL CRP-ADVANCE Multi-Calibrator Set (k060140) is recommended.

This method, using antihuman CRP mouse antibody coated latex to bind CRP, allows for measurement over a wide range of CRP concentrations. The resulting agglutination from binding is measured spectrophotometrically and is proportional to the concentration of CRP in the sample.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Equal Diagnostics', CRP Ultra Wide Range Reagent manufactured by Denka Seiken Co., Ltd.
2. Predicate 510(k) number(s):
k030545
3. Comparison with predicate:

Similarities and Differences		
Item	Device	Predicate
Intended Use	For the quantitative determination of CRP in serum. For In Vitro Diagnostic use	An In Vitro diagnostic test for the determination of CRP in human serum, lithium heparin or EDTA plasma samples by immuniturbidimetry
Materials	R1 – a solution containing a buffer at pH 8.5 R2- a solution containing antihuman CRP mouse monoclonal antibody-coated latex	R1- a Glycine buffer solution R2- Latex suspension – 0.20 w/v% suspension with latex particles sensitized with anti-CRP rabbit antibodies

Similarities and Differences		
Item	Device	Predicate
Methods of Operation	CRP + antihuman CRP mouse monoclonal antibody-coated latex → immune complexes CRP reacts with antihuman CRP mouse monoclonal antibody-coated latex and agglutination occurs. CRP concentration is determined by measurement of the change of absorbance at 570 nm that results from agglutination reaction	CRP in the sample binds to the specific anti-CRP antibody, which has been adsorbed to latex particles and agglutinates. The agglutination is detected as an absorbance change when read on an automated clinical chemistry analyzer (at 570nm) The magnitude of the change is proportional to the quantity of the CRP in the sample.

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

- CLSI - Interference Testing in Clinical Chemistry; Approved Guideline- Second Edition- EP7-A2
- CLSI - Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline - Second Edition - EP9-A2
- CLSI - Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline - EP6-A
- CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline-Second Edition - EP5-A2
- CLSI - Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline - EP17-A

L. Test Principle:

CRP + antihuman CRP mouse monoclonal antibody-coated latex → immune complexes.

CRP reacts with antihuman CRP mouse antibody-coated latex, and agglutination occurs. CRP concentration is determined by measurement of the change of absorbance that results from agglutination reaction.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Within run precision was established by assaying each sample 20 times. Total precision was established by assaying two samples per run, two times per day for 20 days. The results are presented in the table below.

Level		Total SD		Total CV %	Level		Within Run SD		Within Run CV %
mg/L	mg/dL	mg/L	mg/dL		mg/L	mg/dL	mg/L	mg/dL	
1.50	0.150	0.06	0.006	3.7	1.51	0.151	0.03	0.003	1.9
16.06	1.606	0.38	0.038	2.3	15.72	1.572	0.23	0.023	1.5

b. Linearity/assay reportable range:

Linearity of the procedure is up to 360 mg/L on the Hitachi 911. Studies were performed on the Hitachi 911 using samples that ranged from 0.11 to 2.18 mg/L and from 3 to 363 mg/L. The resulting regression equations were $Y = 1.032x - 0.03$ and $Y = 0.996x + 0.06$, respectively.

The reportable range is 0.16 to 360 mg/L on the Hitachi 911.

There was no prozone effect up to 1000 mg/L on the Hitachi 911.

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

The calibrator is traceable to European Reference Materials (ERM) 470 and the assigned values of 3.0, 6.1, 30.0, 181.0 and 362.0 mg/L have been validated by calibrator comparison studies on the Hitachi 911 yielding results of 2.98, 6.12, 30.18, 184.71 and 358.75 mg/L respectively.

d. Detection limit:

The lower limit of quantitation of the procedure described is 0.16 mg/L on the Hitachi 911. A sample containing a low amount of CRP was analyzed forty times on the Hitachi 911. The resulting mean was 0.164 mg/L and CV of 17.3%.

e. Analytical specificity:

Interferences from icterus, lipemia, hemolysis and ascorbic acid were evaluated for the C-reactive protein method on a Hitachi 911 analyzer using a significance criterion of >10% variance from control.

- No significant icteric interference was found at bilirubin levels from 0-50 mg/dL (0-855 μ mol/L).
- No significant lipemic interference was found at Intralipid levels from 0-1000 mg/dL (0-3000 mg/dL triglycerides).
- No significant hemoglobin interference was found at hemoglobin levels from 0- 1000 mg/dL (0-155 μ mol/L).
- No significant ascorbic acid interference was found at ascorbic acid levels from 0-100 mg/dL.

This product has not been tested for HAMA (human anti-mouse antibodies).

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

The performance of this method (y) was compared with the performance of a similar method (x) on a Hitachi 911. Forty patient serum samples ranging from 0.61 to 273.62 mg/L gave a correlation coefficient of 0.9999.

Linear regression analysis gave the following equation:

This method = 0.975 (Hitachi method) + 0.17 mg/L.

The performance of this method (y) was compared with the performance of a similar method (x) on a Hitachi 911. Forty serum samples ranging from 0.64 to 9.33 mg/L gave a correlation coefficient of 0.9979.

Linear regression gave the following equation:

This method = 0.992 (Hitachi method) - 0.027 mg/L.

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:

Less than 3 mg/L from referenced literature (Liuzzo, G., et al., N. Eng. J. Med., 331:417-424, 1994.)

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.