

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k083444

B. Purpose for Submission:

Device modification

C. Measurand:

C-reactive protein in human serum and plasma

D. Type of Test:

Quantitative immunologic assay

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

Proprietary name: Tina-Quant C-Reactive Protein Gen. 3

Common name: CRPL3

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):

Immunoturbidimetric assay for the in vitro quantitative determination of CRP in human serum and plasma on Roche automated clinical chemistry analyzers

2. Indication(s) for use:

Measurement of C-Reactive protein aids in the evaluation of the amount of injury to body tissues.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Roche Hitachi family including: H902, H912, H917, Mod P and Mod D. All analyzers have been previously cleared.

I. Device Description:

The C-Reactive Protein Gen 3 assay is a particle enhance turbidimetric assay consisting of two working reagents. Reagent 1 (R1) is a TRIS buffer with BSA and preservatives and Reagent 2 (R2) consists of Latex particles coated with mouse anti-CRP in glycine buffer, mouse immunoglobulins, and preservative. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The assay is meant to be run on the Roche/Hitachi H902, H912, H917, Mod P, and Mod D family of analyzers. The precipitate is determined turbidimetrically at 570 nm.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Tina-Quant C-Reactive Protein (Latex) (CRPLX)
2. Predicate 510(k) number(s):
k032336
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Immunoturbidimetric assay for the in vitro quantitative determination of CRP in human serum and plasma on Roche automated clinical chemistry analyzers	Same
Calibrator	Preciset Serum Proteins and CFAS Proteins	Same
Controls	CRP T Control N, Precinorm Protein, Precipath Protein	Same
Traceability	Traceable to CRM 470	Same
Reagent Stability	Up to expiration at 2-8° C R1/R2: 84 days opened and refrigerated on the analyzer	Same
Expected Values	<0.5 mg/L	Same

Differences		
Item	Device	Predicate
Instrument Platform	Roche/Hitachi family including H902, H912, H917, Mod P and Mod D	Roche/Hitachi family including H902, H911, H912, H917, Mod P and Mod D
Sample type	Serum, Plasma (Li-heparin and K2/K3-EDTA)	Serum, Plasma (Li-heparin and K2/K3-EDTA), and Sodium citrate
Calibration frequency	After entering new calibrator values, after reagent lot change and as required following quality control procedures	After reagent lot change and as required following quality control procedures
Measuring Range	Roche/Hitachi 901/912/917/Modular P/Modular D analyzers: 0.3-350 mg/L	Roche/Hitachi 902 1-265 mg/L Roche/Hitachi 717/Modular D: 1-265 mg/L 1-398 mg/L with rerun Roche/Hitachi 904/911/912: 1-260 mg/L 1-520 mg/L with rerun Roche/Hitachi 917/Modular P: 1-280 mg/L 1-560 mg/L with rerun

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

Guidance for Industry - Review Criteria for Assessment of C - Reactive Protein (CRP), High Sensitivity C-Reactive Protein (hsCRP) and Cardiac C-Reactive Protein (cCRP) Assays
Guidance for Industry and FDA Staff; Replacement Reagent and Instrument Family Policy
CLSI EP17-A Protocols for Determination of Limits of Detection and Limits of Quantitation

L. Test Principle:

Particle enhanced immunoturbidimetric assay. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The aggregates are determined turbidmetrically.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Within-run precision of the CRPL3 assay was determined using 2 control samples and 3 human samples, run 21 times on the Hitachi 917 analyzer.

Day-to-day precision was determined by three determinations of two controls and three human samples in 1 run/day for 21 days. For the day-to-day precision, the second replicate of the 3-fold determination is used.

	Within Run			Between Run		
Sample	Mean (mg/L)	SD	CV %	Mean (mg/L)	SD	CV %
Control Level 1	3.6	0.03	0.85	3.1	0.08	2.7
Control Level 2	42.2	0.26	0.61	41.4	0.86	2.1
Human Serum 1	0.9	0.03	4.00	0.5	0.03	6.2
Human Serum 2	1.6	0.02	1.02	1.5	0.05	3.3
Human Serum 3	18.4	0.09	0.48	39.1	0.73	1.9

b. *Linearity/assay reportable range:*

To determine the linearity of the CRPL3 test system, three clinical samples were diluted with 0.9% saline in order to cover the measuring range of the assay and were tested on the Hitachi 917. The samples covered theoretical values from 0.13-5.03 mg/L, 0.42-20.591 mg/L, and 3.24-429.39 mg/L and the percent recovery was determined for each region of the measuring range by comparing the measured value of CRP to the theoretical value and shown below:

Region (mg/L)	Percent Recovery (%)
≤ 5	97.3 - 100.56
5 - 350	98.5-101.7
> 350	88.7 – 105.45

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

Traceability: This method is standardized against an internal method traceable to CRM 470 (RPPHS- Reference Preparation for Proteins in Human Serum).

Stability (real-time studies): The unopened kit components are stable up to 12 months stored at 2-8°C. Both reagents are stable opened and refrigerated on the analyzer for 84 days.

d. *Detection limit:*

The limit of blank (LOB) was evaluated on the Hitachi 917 analyzer using 5 replicates of one analyte free sample, run 6 times over ≥ 3 days on 2 instruments. LoB

was determined to be ≤ 0.2 mg/L by calculating the mean value ± 3 SD.

The limit of detection (LOD) and limit of blank (LOB) were according to CLSI EP 17-A guidelines. The LOD was calculated using the standard deviation of 5 samples with low analyte content measured once per run on two instruments and corresponds to the sample concentration which leads with a probability of 95% to a measurement result above the limit of blank. The LOD was calculated to be < 0.2 mg/L from 5 replicates of analyte-free sample on two instruments, with six runs distributed over 3 days.

The functional sensitivity (Limit of Quantitation) for the CRPL3 test system was measured using five low concentration CRP samples in one run/day over 10 days on two analyzers and determined to be 0.6 mg/L.

e. Analytical specificity:

The effect of endogenous interferences was examined by measuring analyte recovery in the presence of hemoglobin, bilirubin, and lipids. No significant interference with CRP measurement was determined with icterus (up to 60 mg/L), hemoglobin (up to 1000 mg/dL), lipids (up to L index of 1000), rheumatoid factor (up to 1200 IU/mL), and no high dose hook effect seen with CRP concentrations up to 1200 mg/L.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The Roche Tina-Quant C-Reactive Protein Gen. 3 assay on a Roche/Hitachi 917 Analyzer (y) was compared to the Roche Tina-Quant CRP (latex) assay on a Roche/Hitachi 917 Analyzer (x) with 67 human serum samples were measured with sample concentrations ranging between 0.22 and 197 mg/L (2.1 -1875 nmol/L). Results of Passing/Bablok and linear regression analyses are summarized below.

Passing/Bablok

$$y = 1.020x - 0.0003$$
$$r = 0.9946$$

Linear regression

$$y = 1.029x - 0.5043$$
$$r = 0.9998$$

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not available

b. Clinical specificity:

Not available

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:

Consensus reference interval for adults: <5 mg/L (<47.6 nmol/L)

Reference: Dati F, Schumann G, Thomas L et al. Consensus of a group of professional societies and diagnostic companies on guidelines for interim reference ranges for 14 proteins in serum based on the standardization against the IFCC/BCR/CAP reference material (CRM 470). Eur J. Clin Chem Clin Biochem 1996;34:517-520.

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.