

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

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

K142993

**B. Purpose for Submission:**

New Device and instrument

**C. Measurand:**

C-reactive protein (CRP)

**D. Type of Test:**

Particle enhanced immunoturbidimetric assay, Quantitative

**E. Applicant:**

Orion Diagnostica, Oy

**F. Proprietary and Established Names:**

QuikRead go® CRP  
QuikRead go® CRP Verification Set  
QuikRead go® CRP Control Set  
QuikRead go® Instrument

**G. Regulatory Information:**

1. Regulation section:

21 CFR §866.5270 – C-Reactive Protein Immunological Test System  
21 CFR §862.1660 – Quality Control Material (Assayed and Unassayed)  
21 CFR §866.2300 – Colorimeter, Photometer, Spectrophotometer for Clinical Use

2. Classification:

Class II – Assay  
Class I – Control and Instrument

3. Product code:

DCK – C-Reactive Protein, Antigen, Antiserum, and Control

JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)  
JJQ – Colorimeter, Photometer, Spectrophotometer for Clinical Use

4. Panel:

Immunology (82) (Assay)  
Clinical Chemistry (75) (Calibrators and Controls)

**H. Intended Use:**

1. Intended use(s):

The QuikRead go® CRP test is an immunoturbidimetric assay for the *in vitro* quantitative determination of C-reactive protein (CRP) in K2-EDTA and lithium heparin whole blood, K2-EDTA and lithium heparin plasma and in serum samples. The test is carried out by means of the QuikRead go® instrument.

Measurement of C-reactive protein aids in the evaluation of injury to body tissues, and infection and inflammatory disorders. The instrument and assay are for use by trained professionals in the clinical laboratory. For *in vitro* diagnostic use only. Not for point-of-care use.

The QuikRead go® CRP Control Set is intended for use as assayed quality-control material for monitoring the performance of the quantitative QuikRead go® CRP assay with the QuikRead go® Instrument. For *in vitro* diagnostic use.

The QuikRead go® CRP Verification Set is designed to be used for calibration verification and for method validation of the QuikRead go® CRP system. This assayed verification material is intended for use with the QuikRead go® CRP test and the QuikRead go® instrument. For *in vitro* diagnostic use.

The Orion Diagnostica QuikRead go® is an *in vitro* diagnostic test system. The QuikRead go® instrument has been designed to measure quantitative test results from patient samples using QuikRead go® reagent kits. Not for point-of-care use.

2. Indication(s) for use:

Same as Intended Use above

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

The QuikRead go® Instrument

**I. Device Description:**

QuikRead go® CRP System consists of the QuikRead go® Instrument, QuikRead go® CRP kit, QuikRead go® CRP Control Set, and QuikRead go® CRP Verification Set.

- QuikRead go® instrument package contains: instrument, instructions for use, power supply, main cable, and certificate of analysis
- QuikRead go® CRP kit contains CRP reagent caps, buffer, capillaries, plungers, and instructions for use. The collection set (capillaries, plungers and instructions) was cleared under K031607.
- QuikRead go® CRP Control Set contains two vials of controls (1mL/vial): Control Low and Control High. QuikRead go® CRP Control Set can be sold separately.
- QuikRead go® CRP Verification Set contains three vials (1 mL/vial) representing low, medium and high level. QuikRead go® CRP Verification Set can be sold separately.

**J. Substantial Equivalence Information:**

1. Predicate device name(s) and 510(k) number(s):

Tina-Quant C-Reactive Protein Gen 3, K083444 (Plasma and serum)  
 ABX CRP REA, K053308 (Whole blood, plasma and serum)

2. Comparison with predicate:

<b>Similarities</b>			
Item	Device QuikRead go® CRP	Predicate Tina-Quant CRP Gen 3	Predicate ABX CRP REA
Intended Use/Indication for Use	Quantitative determination of CRP  Aids in the evaluation of injury to body tissues, and infection and inflammatory disorders.	Quantitative determination of CRP  Aids in the evaluation of the amount of injury to body tissues.	Quantitative, for the in vitro diagnostic testing CRP  Aids in the evaluation of infection, tissue injury and therapy & monitoring of inflammatory disorders
Assay analyte	CRP	Same	Same
Type of assay	Immunoturbidimetric assay	Same	Same
Detection	Photometry	Same	Same
Reference interval	< 5 mg/L	Same	Same

<b>Differences</b>			
Item	Device QuikRead go® CRP	Predicate Tina-Quant CRP Gen 3	Predicate ABX CRP REA
Test principle	Microparticles	Latex particles	Latex particles
Capture antibody	Anti-human CRP F(ab)2 fragment	monoclonal anti-CRP antibodies	anti-CRP polyclonal antibody
Sample type	Whole blood (Li-heparin, K2-EDTA) Plasma (Li-Heparin, K2-EDTA), and Serum	Plasma (Li-Heparin, K2-EDTA, K3-EDTA) and serum	Whole blood, plasma and serum
Instrument	QuikRead go® Instrument.	Roche/Hitachi cobas c systems.	ABX MICROS CRP 200
Traceability	Traceable to the ERM®-DA 474 reference material	Traceable to CRM 470	Traceable to CRM 470
Calibration	The reagents are pre-calibrated. The lot-specific calibration curve is on cuvette	Calibration needed with every reagent lot	Reagent factors for the calibration menu included in the package insert.
Control	2 levels Liquid, Ready to use	Same	Same
Measuring range	5–200 mg/L (plasma and serum) 5–150 mg/L (whole blood)	0.3–350 mg/L	0–150 mg/L (plasma) 0–200 mg/L (whole blood)

#### QuikRead go® Instrument

<b>Similarities and Differences</b>			
Item	Device QuikRead go®	Predicate Roche/Hitachi cobas c system	Predicate ABX MICROS CRP 200
Intended Use/Indication for Use	<i>In vitro</i> diagnostic test system. The QuikRead go® instrument has been designed to measure quantitative test results from patient samples using	Automated clinical analyzer to quantitative measurement of patient samples.	For the <i>in vitro</i> diagnostic testing of whole blood & plasma specimens. The device operates in complete blood count (CBC) mode or in CBC & C-reactive

<b>Similarities and Differences</b>			
<b>Item</b>	<b>Device QuikRead go®</b>	<b>Predicate Roche/Hitachi cobas c system</b>	<b>Predicate ABX MICROS CRP 200</b>
	QuikRead go® reagent kits.		protein (CRP) mode.
Detection	Photometer	Same	Same
Sample operation	Manual sample addition and reagent cap insertion	Fully automated	Fully automated
Sample volume	20 µL	2 µL	18 µL
Calibration frequency for CRP assay	The instrument reads lot-specific barcode from the cuvette label and save the calibrations into the instrument memory	Analyzer-specific calibration needed with C.f.a.s Proteins with every reagent lot change	Package labeling contains the CRP reagent factors for the calibration menu, when replacing CRP reagents

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

- CLSI EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Second Edition.
- CLSI EP6-A, Evaluation of Linearity of Quantitative Measurement, Approved Guideline, Second Edition.
- CLSI EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition
- CLSI EP09-A3, Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline, Second Edition (Interim Revision).
- CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline, Second Edition
- CLSI LIS02-A2, Standard Specification for Transferring Information between Clinical Instruments and Computer Systems; Approved Standard-Second Edition
- CLSI LIS01-A2, Standard Specification for Low-Level Protocol to Transfer Messages between Clinical Laboratory Instruments and Computer Systems
- IEC 61010-1, Safety Requirements for Electrical Equipment for Measurement, Control and Laboratory Use – Part 1, 2001.
- IEC 61326-1, Electrical Requirements for Measurement, Control and Laboratory Use – EMC Requirements – Part 1: General Requirements, 2005
- 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 Off-the-Shelf Software Use in Medical Devices; Final
- General Principles of Software Validation; Final Guidance for Industry and FDA Staff

- Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices - Guidance for Industry and FDA Staff

**L. Test Principle:**

QuikRead go® CRP is an immunoturbidimetric test based on an agglutination reaction. Microparticles are coated with anti-human CRP F(ab)2 fragments, and the CRP present in the sample reacts with the microparticles. The resultant change in the turbidity of the solution is measured by the QuikRead go® instrument.

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

1. Analytical performance: All results presented below were within the sponsor’s pre-determined acceptance criteria for each study.

*a. Precision/Reproducibility:*

Precision: The precision of the QuikRead go® CRP assay was evaluated by testing four K2-EDTA plasma samples containing various concentrations of CRP per CLSI EP05-A3. Each sample was run in duplicate, twice a day, for 20 days with one reagent lot (total of 80 replicates per sample). One additional sample with a CRP concentration level near 5 mg/L was tested with the same protocol but with two different reagent lots. The results are summarized in the table below.

		Within-Run		Between-Run		Between-Day		Total	
Sample	Mean (mg/L)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
1	5.0	0.4	8.8	0.4	7.2	0.1	2.1	0.6	11.6
2	10.1	0.3	2.8	0.2	1.6	0.1	1.2	0.3	3.4
3	19.3	0.3	1.7	0.3	1.5	0.2	1.3	0.5	2.6
4	50.8	0.4	0.8	0.5	1.0	0.3	0.5	0.7	1.4
5	107.0	1.6	1.5	0.6	0.6	1.2	1.2	2.1	2.0

Reproducibility: To evaluate lot-to-lot reproducibility, three K2-EDTA plasma samples with CRP concentration at low (9.9 mg/L), medium (50.9 mg/L), and high (107.1 mg/L) were tested. Each sample was tested in replicates of five, one run per day for five days using three difference reagent lots. %CV values for between-lot reproducibility were 8.9%, 1.9% and 1.8% for samples with low, medium and high level CRP, respectively.

Site-to-site reproducibility was tested with three K2-EDTA plasma samples at three sites using one reagent lot. At each site, samples were run in replicates of five, once a day, for five days, to generate 25 data points for each sample. Data were analyzed for repeatability, within-laboratory precision and site-to-site reproducibility. The results are summarized in the table below:

Sample	N	Mean (mg/L)	Repeatability		Within-Lab Precision		Site-to-Site Reproducibility	
			SD	CV (%)	SD	CV (%)	SD	CV (%)
1	75	10.8	0.5	4.6	0.8	7.8	0.8	7.8
2	75	52.1	0.7	1.3	1.0	1.8	1.4	2.7
3	75	100.9	1.5	1.5	3.0	2.9	6.0	6.0

b. *Linearity/assay reportable range:*

Linearity: The linearity across the measuring range of the assay was evaluated by a study according to CLSI EP6-A. Eleven serially diluted samples were prepared by diluting a high positive K2-EDTA plasma sample (148.5 mg/L) with a low K2-EDTA plasma sample (4.0 mg/L). Each dilution sample was tested in replicate of four. The linearity study was also performed with the same protocol using a dilution series prepared with a high positive K2-EDTA whole blood sample (246.8 mg/L) and a low K2-EDTA whole blood sample (4.5 mg/L). The results of % recovery and linear regression analysis are shown below:

Test Range (mg/L)	Slope (95% CI)	Intercept (95% CI)	R2	% Recovery
<i>K2-EDTA plasma sample</i>				
4.0–148.5	1.03 (1.02–1.05)	-1.18 (-2.64–0.29)	1.00	94–105%
<i>K2-EDTA whole blood sample</i>				
4.5–246.8	1.04 (1.02–1.06)	-1.39 (-4.15–1.38)	1.00	95–105%

The claimed measuring range for the QuikRead go® CRP is 5–120 mg/L when using K2-EDTA plasma sample and 5–150 mg/L when using whole blood sample.

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

Traceability:

The calibrators used to calibrate the QuikRead go® CRP test are traceable to the ERM®-DA 474 reference material.

Controls and Verification Set:

The calibrator materials are traceable to the ERM-DA 474 reference material and are used to generate the standard curve for QuikRead go® CRP kit. The value assignment for each level of the verification set and control set is done by testing each manufacturing material 10 runs per day for two days on two QuikRead go® Instruments using a minimum of three lots of QuikRead go® CRP kit with two operators. The mean of results is assigned to each level of the QuikRead go® CRP verification set and controls. The target value and range for QuikRead go® CRP calibrators and controls are shown below:

	<b>Target Value (mg/L)</b>	<b>Target Range (mg/L)</b>
<i>QuikRead go® CRP Verification Set</i>		
Calibrator 1	10	9–13
Calibrator 2	50	45–50
Calibrator 3	90	85–95
<i>QuikRead go® CRP Controls</i>		
Control Low	30	25–35
Control High	80	70–100

**Stability:**

***Kit stability:*** Real-time stability was tested for unopened and opened QuikRead go® CRP kit reagent, controls and verification set respectively. The stability results are as follows:

<b>Kit component</b>		<b>Storage 2–8°C</b>	<b>Storage 18–25°C</b>
CRP Reagent caps	Opened	15 months	1 month (24 hour/day) 3 month (7.5 hour/day)
	Unopened	15 months	1 month (24 hour/day) 3 month (7.5 hour/day)
Pre-filled cuvettes	Unopened with the foil pouches	15 months	15 months
	Unopened without the foil pouches	6 months	3 months
	Opened	2 hours	2 hours
Verification Sets	Unopened	24 months	N/A
	Opened	21 days	N/A
Controls	Unopened	24 months	N/A
	Opened	1 month	N/A

***Sample stability:*** The study was performed for all sample types. For each sample type, three samples with different CRP concentration levels (low, medium, high) were stored at 2–8°C. In addition, the samples were tested for the stability when stored in buffer at 18–25°C. The claimed sample stability is summarized in the table below:

<b>Sample type</b>	<b>Storage</b>
Anticoagulated whole blood (K2-EDTA and Li-heparin)	3 days at 2–8°C
Plasma (K2-EDTA and Li-heparin)	7 days at 2–8°C
Serum	7 days at 2–8°C
Sample in buffer	2 hours at 18–25°C

*d. Detection limit:*

The Limit of Blank (LoB) was determined by assaying six blank samples in 10 replicates per sample over three days with two reagent lots. A total of 60 data points per lot were generated. LoB for each lot was calculated separately at the 95th percentile. The LoB was determined to be 1.1 mg/L and 1.2 mg/L for each lot respectively. The claimed LoB value is 1.2 mg/L.

Limit of Detection (LoD) was determined by assaying six K2-EDTA plasma samples with low CRP level. Each sample was tested in 10 replicates over three days with two reagent lots. LoD value was calculated as the LoB + 1.645xSD of the replicates for the low level samples. The LoD for the two lots were determined to be 1.8 mg/L and 1.9 mg/L, respectively. The claimed LoD for the assay is 1.9 mg/L.

Limit of Quantitation (LoQ) was determined based on CLSI EP17-A2 by further testing seven K2-EDTA plasma samples with low level of CRP. Each sample was tested with a replicates of 10 over three days with two reagent lots. The LoQ was determined as the lowest sample concentration that meets the accuracy goal of TE(%)  $\leq 20\%$  and was found to be 3.6 mg/L.

The lower limit of the measuring range claimed for QuikRead go® CRP is 5 mg/L.

*e. Analytical specificity:*

Interference studies were performed according to CLSI EP7-A2 using three K2-EDTA samples with CRP concentrations around 10, 50, and 100 mg/L. For rheumatoid factor interference, additional sample with CRP concentration around 20 mg/L was tested. Each sample was spiked with six different levels of potential interfering substances and tested in replicates of three. The recovery was calculated by comparing to control samples spiked with the same volume of diluents

<b>Interfering Substances</b>	<b>Concentration</b>	<b>Range of Recovery</b>
Bilirubin	230 mg/L (400 $\mu$ mol/L)	99%–106%
Vitamin C	35 mg/L (200 $\mu$ mol/L)	97%–104%
Hemoglobin	2000 mg/dL	98%–109%
Triglycerides	10 g/L (11.5 mmol/L)	98%–105%
Rheumatoid factor	525 IU/mL	100%–102%

*f. Assay cut-off:*

See the reference range/expected value.

2. Comparison studies:

a. *Method comparison with predicate device:*

Method comparison with Tina-Quant CRP Gen 3: Two studies were performed. In the first study, 97 clinical K2-EDTA plasma samples were tested with QuikRead go® CRP and the predicate Tina-Quant CRP Gen 3. The second study was similar and tested 62 K2-EDTA plasma clinical samples. The Deming regression analysis was performed for both studies by comparing the results obtained from QuikRead go® CRP and Tina-Quant CRP Gen 3 for these two studies. The results are summarized below:

	<b>N</b>	<b>Range (mg/L)</b>	<b>Slope (95% CI)</b>	<b>Intercept (95% CI)</b>	<b>R2</b>
Study 1	97	6.1–110.8	1.07 (1.05–1.10)	-1.47 (-2.13– -0.81)	1.00
Study 2	62	8.6–120.2	1.01 (0.99–1.03)	-0.24 (-0.97–0.50)	1.00

Method comparison with ABX CRP REA on ABX Micros CRP 200: The same 62 K2-EDTA plasma samples from above study 2 were also tested with predicate ABX CRP on ABX Micros CRP 200 instrument. In addition, samples of 68 K2-EDTA whole blood samples were assayed with QuikRead go® CRP and ABX CRP REA to demonstrate the performance of QuikRead go® CRP when using whole blood samples. The Deming regression analysis comparing the results obtained from QuikRead go® CRP and ABX CRP REA for each sample type is summarized below:

<b>N</b>	<b>Range (mg/L)</b>	<b>Slope (95% CI)</b>	<b>Intercept (95% CI)</b>	<b>R2</b>
<i>K2-EDTA plasma samples</i>				
62	8.0–114.0	1.02 (0.98–1.06)	-2.65 (-4.07– -1.24)	1.00
<i>K2-EDTA whole blood samples</i>				
68	7.1–151.8	0.90 (0.86–0.95)	-2.98 (-5.10– -0.87)	0.98

b. *Matrix comparison:*

Potential differences between sample matrices (serum, Li-heparin plasma, K2-EDTA plasma, Li-heparin whole blood, K2-EDTA whole blood) were evaluated by testing 68 patient samples in each of the five matrices from 68 individual subjects (340 total samples) using one lot of QuikRead go® CRP reagent. Sample concentrations spanned the assay ranges. Each set of samples was tested in singlet on QuikRead go® instrument. Among these samples, 62 sets of samples had CRP values within the measuring range of assay and were performed with a Deming regression analysis. The results are presented in the following table:

<b>n=62 (QuikRead go®)</b>	<b>Test Range (mg/L)</b>	<b>Slope (95% CI)</b>	<b>Intercept (95% CI)</b>	<b>R2</b>
K2-EDTA plasma vs. K2-EDTA whole blood	7.0–118.0	0.96 (0.94–0.99)	-1.24 (-2.05– -0.44)	0.99
K2-EDTA plasma vs. Li-heparin whole blood	7.0–118.0	0.94 (0.91–0.98)	-1.26 (-2.31– -0.21)	0.99
K2-EDTA plasma vs. Li-heparin plasma	7.0–118.0	0.97 (0.95–0.99)	0.31 (-0.35–0.98)	1.00
K2-EDTA plasma vs. Serum	7.0–118.0	0.95 (0.94–0.97)	0.42 (-0.15–0.99)	1.00

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 reference range is  $\leq 5$  mg/L in apparently healthy individuals (*Dati F, et al. 1996., 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.34:517-520*). The clinical cut-off for conventional CRP assays is approximately  $\leq 10$  mg/L per 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.

The reference range in the normal population was verified by analyzing CRP concentration in a cohort of 143 apparently healthy blood donors (59 males and 84 females, ages from 19 to 65 years, with an average age of 42.7 years and median age of 42 years) using QuikRead go® CRP. The results (for K2-EDTA samples) are summarized as follows:

	<b>Total (n=143)</b>	<b>Male (n=59)</b>	<b>Female (n=84)</b>
Mean	1.6 mg/L	1.5 mg/L	1.6 mg/L
Median	1.4 mg/L	1.4 mg/L	1.4 mg/L
95% percentile	3.7 mg/L	3.1 mg/L	3.9 mg/L
99% percentile	5.9 mg/L	3.7 mg/L	5.7 mg/L

It is recommended that each laboratory establishes its own reference range for the population in its region.

**N. Instrument Name:**

QuikRead go® Instrument

**O. System Descriptions:**

1. Modes of Operation:

Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

Yes \_\_\_\_\_ or No  \_\_\_\_\_

Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

Yes \_\_\_\_\_ or No  \_\_\_\_\_

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:

Samples are identified manually. The instrument has a built-in connection for a barcode reader for future applications.

4. Specimen Sampling and Handling:

Only the capillaries and plungers included in the QuikRead go® CRP kit are recommended for adding the sample to a prefilled cuvette. 20 µL of blood sample taken by a capillary is dispensed into the buffer solution in the cuvette by pressing down the plunger. The cuvette is closed tightly with a CRP Reagent Cap without shaking. The

cuvette is then placed in the instrument for measurement.

5. Calibration:

The reagents are pre-calibrated. The lot-specific calibration curve is coded into the two-dimensional barcode label on the side of the each pre-filled cuvette. In addition, the barcode contains reagent lot information (reagent cap lot and buffer lot) and expiry date information and parameters (which are not lot-specific) for hematocrit calculation. This barcode is read automatically by QuikRead go® instrument and information is saved into the instrument memory.

6. Quality Control:

Quikread CRP control is made for Orion Diagnostica by Sero AS, Norway. The following information is provided: description of matrix and the manufacturing process, value assignment, stability protocol, certificate of origin, and certificate of analysis.

**P. Other Supportive Instrument Performance Characteristics Data Not Covered In The “Performance Characteristics” Section above:**

N/A

**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.