

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

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

k120626

**B. Purpose for Submission:**

New device

**C. Measurand:**

Calcium

**D. Type of Test:**

Quantitative photometric method

**E. Applicant:**

Vital Diagnostics

**F. Proprietary and Established Names:**

Eon Calcium Reagent

**G. Regulatory Information:**

Measurand	Regulation Section	Classification	Product Code	Panel
Calcium	21CFR862.1145	Class II	CJY	(75) Clinical Chemistry

**H. Intended Use:**

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

Vital Diagnostics Eon Calcium Reagent is a device intended to measure the total calcium level in serum or plasma on an Eon 100 Analyzer. Calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

Eon 100 clinical chemistry analyzer.

**I. Device Description:**

The Eon Calcium Reagent kit includes 4 x 22 mL bottles of Eon Calcium Reagent. The Reagent contains > 0.13mmol/L arsenazo III, buffer, surfactants, sodium azide and other non-active ingredients.

**J. Substantial Equivalence Information:**

1. Predicate Device Name(s):  
Roche Calcium (Ca) Reagent
2. Predicate 510(k) number(s):  
k871811
3. Comparison with predicate:

<b>Similarities and Differences</b>		
Item	Eon Calcium Reagent Candidate Device (k120626)	Roche Calcium (Ca) Reagent Predicate Device (k871811)
Intended Use/Indications for Use	Same	In vitro test for the quantitative determination of calcium
Specimen Type	Serum and Plasma	Serum, Plasma, and Urine
Instrument	Eon 100 clinical chemistry analyzer	Roche automated clinical chemistry analyzers
Expected values in Serum	8.6 -10.2 mg/dL	8.4 – 10.2 mg/dL
Measuring range (Serum /Plasma)	1.3 - 16 mg/dL	0.2-16 mg/dL
Reagent Configuration	Single part liquid	Two part liquid
Reagent Stability	Unopened: 2-8°C until expiration date  On board stability: 28 days	Unopened: 2-8°C until expiration date  On board stability: 42 days Reagent 1 90 days Reagent 2
Calibration Stability	28 days	3 days

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

- CLSI Guideline, EP5-A2 *Evaluation of Precision Performance of Clinical Chemistry Devices – Second Edition*
- CLSI Guideline, EP6-A2 *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach*
- CLSI Guideline, EP17-A2 *Protocols for Determination of Limits of Detection and Limits of Quantitation*
- CLSI Guideline, EP9-A2 *Method Comparison and Bias Estimation Using Patient Samples; Approved Guidelines - Second Revision (Interim Revision)*

**L. Test Principle:**

The Eon Calcium reagent employs a colorimetric method which is based on the binding of calcium by arsenazo III to form a blue complex that absorbs at 630 nm. This absorbance change is proportional to the calcium concentration of the sample.

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

1. Analytical performance:

All the performance studies were conducted using the Eon 100 clinical chemistry analyzer.

a. *Precision/Reproducibility:*

Precision was evaluated according to the CLSI Document EP5-A2, *Evaluation of Precision Performance of Quantitative Measurement Methods*. Studies were carried out over a period of 21 days (42 runs) using three levels of control serum. Two runs per day were carried out on a single reagent lot on one Eon 100 analyzer. The following Precision data (Within Run and Total) were obtained.

	Total Precision				Within Run			
	N	Mean (mg/dL)	SD	% CV	N	Mean (mg/dL)	SD	% CV
Level 1	84	8.33	0.14	1.7	84	8.33	0.10	1.2
Level 2	84	11.11	0.14	1.2	84	11.11	0.10	0.9
Level 3	84	15.07	0.21	1.4	84	15.07	0.12	0.8

b. *Linearity/assay reportable range:*

The measuring range of the assay for serum is 1.3 – 16.0 mg/dL (0.325 – 4.00 mmol/L). Ten dilutions of a stock standard were prepared to exceed the target linearity claim (16 mg/dL) using commercially available materials. Calcium levels were measured in duplicates. The measured vs. expected linear regression analysis resulted in a following linear regression parameters:

Lowest and the highest concentration tested	Intercept	Slope	r2
1.3 – 20.7 mg/dL	- 0.936	1.058	0.9990

Based on the linearity study results, the sponsor claimed that the assay's measuring range is 1.3 to 16.0 mg/dL.

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*  
Vital Serum Calibrator has an assigned calcium value traceable to NIST Standard Reference Material (SRM) 915b.

Eon Calibrators were cleared in k110394  
Eon Serum Controls were cleared in k111063

The sponsor performed reagent stability studies and protocol and acceptance criteria were reviewed and found to be adequate. Accelerated stability studies were performed to simulate 24 months stability of the reagent when stored at 2°C to 8°C. Real time stability studies are on-going.

- d. *Detection limit:*

Studies were carried out in accordance with CLSI Guidance Document EP17-A: *Protocols for Determination of Limits of Detection and Limits of Quantitation*. The detection of Limit of the Blank (LoB) and Limit of Detection (LoD) were performed using 60 blank and 60 low level samples. The samples were measured using two reagent lots on two Eon 100 analyzers. LoB and LoD were calculated using the following equations:  
Limit of Blank (LoB) = Mean blank + 1.645 x (SD blank)  
Limit of Detection (LoD) = LoB + 1.645 x (SD low level sample)

For the purposes of determining LoB, the mean blank result was a negative value (-0.189) and was rounded up to zero

Based on results of this study, the following claims for LoB and LoD are made:

LoB = 0.1 mg/dL

LoD = 0.3 mg/dL.

The sponsor's claimed measuring range is 1.3 to 16.0 mg/dL.

- e. *Analytical specificity:*

The sponsor performed studies to evaluate effect of endogenous interferences for icterus (conjugated and unconjugated bilirubin), hemolysis (hemoglobin), lipemia (intralipids), and exogenous compounds on the performance of the Eon Calcium Reagent assay, following CLSI EP7-A2, *Interference Testing in*

*Clinical Chemistry; Approved Guideline.*

Testing was performed with serum samples in the presence of two levels of Calcium and different concentrations of the endogenous and exogenous compounds. Percent recovery was calculated relative to control samples containing Calcium without spiked compounds. The sponsor defines non-significant interference as <10% difference between the spiked and the non-spiked samples. Based on the results, the sponsor concludes no significant interference for the following endogenous substances:

Hemoglobin up to 1000 mg/dL (10 g/L)  
Lipemia (Intralipid® measured as Triglycerides) up to 500 mg/dL  
Bilirubin up to 30 mg/dL (513 µmol/L)

Exogenous substances listed below were tested at 2 concentrations (low and high) and the sponsor concludes no significant interference ( $\pm 10\%$ ) in calcium recovery in the presence of:

Ascorbic Acid up to 4 mg/dL (227µmol/L)  
Acetylsalicylic Acid up to 60 mg/dL (3.3 mmol/L)  
Acetaminophen up to 25 mg/dL (1.6 mmol/L)

In addition the sponsor cites literature in the labeling regarding other potential drug interference <sup>1</sup>

1. Young S. Effects of drugs on clinical laboratory tests. 5th Ed. Washington DC: AACC press; 2000

f. *Assay cut-off:*  
Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

The sponsor performed studies to compare the performance of the Eon Calcium assay (y) with a predicate method on Roche Hitachi 911 (x) based on CLSI EP9-A2 guidelines. A total of 62 human serum samples from which 3 samples were spiked and 8 diluted were assayed in the range from 2.2 to 15.1 mg/dL. The comparison by Deming regression resulted in a slope of 1.054 (95%CI = 1.015 to 1.094), an intercept of -0.265 (95%CI = -0.638 to 0.109), correlation coefficient of  $R^2 = 0.9787$ , and a std. error of 0.328.

b. *Matrix comparison:*

The sponsor performed a matrix study to compare the performance of the

assay when different sample types/tubes (serum vs. Lithium Heparin plasma) were tested. Parallel drawn (matched) serum and plasma (Lithium Heparin) samples from 49 individuals were assayed and the results compared by regular and Deming regression. A total of 49 samples contained 4 diluted and 4 spiked samples. Duplicate samples were tested in the range of 1.4 to 14.2 mg/dL. Samples were analyzed on one Eon 100 analyzer and using one Eon Calcium Reagent. Each plasma sample was compared to the respective serum sample. Results of regression analysis are summarized below:

Regression analysis	n	Range (mg/dL)	Regression Equation	Correlation Coefficient (R <sup>2</sup> )	Standard Error	Confidence Interval Slope	Confidence Interval Intercept
Regular	49	1.4 to 14.2	$y = 1.026x - 0.405$	0.9761	0.336	0.978 to 1.073	- 0.867 to - 0.058
Deming	49	1.4 to 14.2	$y = 1.038x - 0.529$	0.9761	0.337	0.991 to 1.086	- 0.993 to - 0.065

The sponsor claims that Lithium heparin is an acceptable anticoagulant to be used with the Eon Calcium assay.

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:

8.6 – 10.2 mg/dL (2.15 – 2.55 mmol/L)<sup>1</sup>

The quoted range should serve as a guide only. It is recommended that each laboratory verifies this range or establishes a reference interval for the population that it services.<sup>1</sup>

1. Wachtel M, Paulson R, Plese C. Creation and verification of reference

intervals. Lab Med 1995; 26: 593-7.

**N. Proposed Labeling:**

The labeling is sufficient and does satisfy 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.