

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

A. 510(k) Number:

k041009

B. Purpose for Submission:

New product

C. Analyte:

Calcium

D. Type of Test:

Quantitative colorimetric assay

E. Applicant:

Hemagen Diagnostics Inc.

F. Proprietary and Established Names:

Raichem Calcium (oCPC) Reagent (liquid); Calcium Reagent

G. Regulatory Information:

1. Regulation section:
21 CFR §862.1145: Calcium test system
2. Classification:
Class II
3. Product Code:
CIC
4. Panel:
Chemistry (75)

H. Intended Use:

1. Intended use/Indication(s) for use:
“This reagent is intended for the quantitative determination of Calcium in serum, heparinized plasma, or urine. For in vitro diagnostic use only.

This calcium test system is a device intended to measure the total calcium level in serum. 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). The intended patient population may be adult, pediatric, and neonatal.”

2. Special condition for use statement(s):
This product is for prescription use only.

3. Special instrument Requirements:
Roche COBAS Mira Chemistry System

I. Device Description:

The device consists of two liquid reagents. Reagent 1 contains ethanolamine, buffers, stabilizers, and fillers while Reagent 2 contains o-cresolphthalein (oCPC), 8-quinolinol, buffers, stabilizers, and fillers. The reagents are ready for use.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Raichem Calcium (oCPC) Powder Reagent
2. Predicate K number(s):
k843353
3. Comparison with predicate:
Raichem Calcium Liquid Reagent is similar, or identical, to the listed predicate in the following ways: both products have the same intended use, utilize the enzymatic reactions on the same instrument, have the same analytic range, use the matrices, and have the same stability. The proposed product has been modified from a dry powder to a format consisting of two liquid components, optimized for stability.

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

Area of Study	Reference Procedure	Procedure Title
Method Comparison/ Anticoagulant Studies	NCCLS EP9-A	User Comparison of Quantitative Clinical Laboratory Methods Using Patient Samples
Precision	NCCLS EP5-A	User Evaluation of Precision Performance of Clinical Chemistry Devices
Linearity	NCCLS EP6-A	Evaluation of the Linearity of Quantitative Methods
Interferences/ Cross-Reactivity	NCCLS EP7-A	Interference Testing in Clinical Chemistry
Guidance	FDA (Draft)	"Data for commercialization of original equipment manufacturer, secondary, and generic reagents for automated analyzers, 10 June 1996"

L. Test Principle:

The test is based on the production of a colored complex when calcium reacts with oCPC. The color intensity of the solution of the dye is proportional to the concentration of calcium in serum.

M. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*

Precision studies to support the serum claim were performed according to NCCLS EP5-A guidelines; two studies tested two levels of controls 20 times in one day, and a separate study was performed over 20 days, two runs per day, with two levels of Raichem quality controls tested in duplicate. Only within-run precision was measured for urine since the performance during the within-run testing was very similar to the performance of serum during both with-in tests. The sponsor set acceptance criteria as ≤ 0.3 SD for both matrices.

Precision of Raichem Calcium Liquid Reagent with Serum

Level	Assay Values		Mean (mg/dL)	Within Run*		Total Imprecision	
	Min	Max		Std Dev	% CV	Std Dev	% CV
Normal	8.40	9.20	8.78	0.09	1.0	0.19	2.1
Abnormal	12.0	12.9	12.50	0.12	1.0	0.23	1.8

* Within run data shown here is compiled from the Total Imprecision testing. These results are comparable to the results obtained in both separate within run tests described above.

Precision of Raichem Calcium Liquid Reagent with Urine

Level	Assay Values		Mean (mg/dL)	Within Run	
	Min	Max		Std Dev	% CV
Normal	4.3	4.6	4.5	0.10	2.2
Abnormal	13.4	14.0	12.5	0.13	0.9

The sponsor tested accuracy by assaying two levels of control material in duplicate. Acceptance criteria were based on whether the results were within the specified range of the controls.

Control Recovery (mg/dL) by Raichem Calcium Reagent

	Range	Mean Results
Assayed Serum Control 1	8.1 – 10.1 mg/dL	9.0 mg/dL
Assayed Serum Control 2	11.2 – 13.6 mg/dL	12.3 mg/dL

b. *Linearity/assay reportable range:*

NCCLS EP6-A guidelines were used to design this study. To support the serum claim, five pre-diluted commercially supplied linearity levels were read four times. To support the urine claim, dilutions of

spiked urine were read four times. Recovery was calculated from the assay mean; all recoveries were within the manufacturer's specification of 95% to 105% of the assigned value of the diluted sample (serum, $y=0.991x + 0.090$, $r^2 = 0.997$; urine, $y=1.015x + 0.012$, $r^2 = 0.999$). The data supports the claim of linearity to 15 mg/dL.

c. *Traceability (controls, calibrators, or method):*
None provided.

d. *Detection limit:*
Water was assayed twenty times in a single analytical run. The detection limit is calculated as the mean (or zero if the mean is less than zero) plus two standard deviations of the results. The observed mean and standard deviation was 0.02 and 0.04 mg/dL respectively. Therefore, the detection limit of the assay is 0.08 mg/dL calcium.

e. *Analytical specificity:*
Clear, unhemolyzed serum, heparinized plasma, and urine are acceptable matrices; **do not** use plasma prepared using EDTA, oxalate, or citrate, which function by removing calcium.

Interference effects of several substances, including some endogenous compounds, were tested on the Cobas Mira. Results are presented as percent variance sample of the highest concentration tested from an unaltered serum.

Interferent's Effect on Raichem Calcium (o-CPC) Assay

Interferent	Concentration Tested	% Variance
Bilirubin (Free)	60 mg/dL	-17.1
Bilirubin (Conjugated)	60 mg/dL	-2.4
Omniscan (gadodiamide)	2.5 mg/dL	-27.3
Hemoglobin	1000 mg/dL	-5.3
Intralipid	1000 mg/dL	-14.9
Magnesium (low conc)	5.3 mg/dL	0
Magnesium (hi conc)	20 mg/dL	2.4
Magnesium (hi serum conc)	20 mg/dL	0

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

2. Comparison studies:

a. *Method comparison with predicate device:*

Method comparison studies were based on NCCLS 9A. The sponsor tested 131 serum samples ranging from 0.45 to 14.5 mg/dL in duplicate using Roche Calcium (Arsenazo III) Reagent and the proposed Raichem Calcium reagent on a Cobas MIRA analyzer.

Urine samples (n=54) ranging from 0.29 to 30.5 mg/dL were compared by using values obtained from the predicate method (oOPC) tested on a Hitachi 717 analyzer and the proposed Raichem reagent tested on a Cobas MIRA analyzer. Samples above the assay range were auto-diluted and retested. Regression statistics are shown below; all are within the manufacturer's specifications.

Comparison of Raichem Calcium Reagent and Predicates

Value	Serum	Urine
Method	Arsenazo III v. oOPC	oOPC v. oOPC
Slope	1.017	1.008
Intercept	0.013 mg/dL	0.00 mg/dL
R ² value	0.981	0.998
N	131	54
Range	0.45 – 14.5 mg/d	0.29 – 30.5 mg/dL

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:

Tietz reports a normal reference range of 8.5 – 10.5 mg/dL serum calcium (Fundamentals of Clinical Chemistry).

N. Conclusion:

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