

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

A. 510(k) Number:

k041643

B. Purpose For Submission:

Premarket Notification 510(k) of intention to manufacture and market the Beckman Coulter SYNCHRON Systems Phosphorus Reagent.

C. Analyte:

Inorganic Phosphorus

D. Type of Test:

Quantitative

E. Applicant:

Beckman Coulter, Inc.

F. Proprietary and Established Names:

SYNCHRON® Systems Phosphorus (PHS) Reagent.

G. Regulatory Information:

1. Regulation section:
21 CFR §862.1580, Phosphorous (inorganic) test_system.
2. Classification:
Class I
3. Product Code:
CEO
4. Panel:
75 Chemistry

H. Intended use(s):

1. Intended use(s)

The SYNCHRON® Systems Phosphorous (PHS) Reagent, in conjunction with SYNCHRON® Multi Calibrator, is intended for use in the quantitative determination of inorganic phosphorous in human serum, plasma, or urine.

Measurements of phosphorous (inorganic) are used in the diagnosis and treatment of various disorders, including parathyroid gland and kidney diseases, and vitamin D imbalance.

2. Indication(s) for use:

The SYNCHRON® Systems Phosphorous (PHS) Reagent, in conjunction with SYNCHRON® Multi Calibrator, is intended for use in the quantitative determination of inorganic phosphorous in human serum, plasma, or urine.

Measurements of phosphorous (inorganic) are used in the diagnosis and treatment of various disorders, including parathyroid gland and kidney diseases, and vitamin D imbalance.

3. Special condition for use statement(s):

For Prescription Use.

4. Special instrument Requirements:

The SYNCHRON Systems PHS Reagent is intended for use on the following models of SYNCHRON Systems: SYNCHRON LX®, LX PRO, LXi 725, CX®4CE, CX4 DELTA, CX4 PRO, CX5CE, CX5 DELTA, CX5 PRO, CX7, CX7 DELTA, CX7 RTS, CX7 PRO, CX9 ALX, and the CX9 PRO all of which have been previously cleared by the FDA 510(k) process. A summary of the 510(k) history for the instrumentation is provided in the table below:

System	FDA Docket #
SYNCHRON CX4CE	k904220
SYNCHRON CX7 SYNCHRON CX7 RTS (Add to File)	k904219
SYNCHRON CX5CE	k926060
SYNCHRON CX DELTA (CX4Δ, CX5Δ CX7Δ) SYNCHRON CX9 ALX (Add to File)	k950958
SYNCHRON LX20	k965240
SYNCHRON LX20 PRO	k011213
SYNCHRON CX PRO (CX4PRO, CX5PRO,CX7PRO,CX9PRO)	k011465
SYNCHRON LXi 725	k023049

I. Device Description:

The SYNCHRON Systems PHS reagent is designed for optimal performance on the SYNCHRON CX (CX4CE/4Δ/4PRO, CX5CE/5Δ/4PRO CX7CE/7Δ/7PRO, CX9ALX/9PRO) AND LX (LX20/PRO/LXi 725) Systems. The ready to use liquid reagent kit contains two PHS 300 test cartridges. The cartridges are packaged separately from the associated calibrator.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Beckman Coulter Inc. SYNCHRON Systems PO4 Reagent.
2. Predicate k number(s):
(k883181)
3. Comparison with Predicate:

Similarities between the Synchron Systems PHS Reagent and the predicate device are summarized below:

Reagent	Aspect / Characteristic	Comments
Synchron Systems PHS Reagent	Intended Use	Same as Beckman Coulter's Synchron Systems PO4 Reagent
	Methodology	
	Reactive Ingredients	
	Sample Types	
	Detection Wavelength	
	Reaction Volumes (sample, reagent)	
	Shelf Life	

Differences between the candidate and predicate products are summarized below:

Reagent	Aspect / Characteristic	Comments
Synchron Systems PHS Reagent	Non-reactive Ingredients	PHS: Optimized formulation PO4: Original formulation
	Reaction Type (endpoint)	PHS: Sample-blanked PO4: Reagent-blanked
	TCA precipitation method (for serum proteins)	PHS: Compatible PO4: Incompatible
	Instrument Platforms	PHS: CX CE / Δ / PRO and LX20 / PRO / LXi Systems PO4: CX Systems Only

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

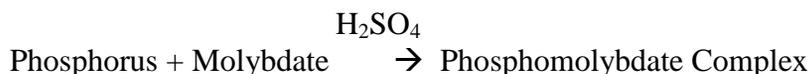
NCCLS EP5-A, NCCLS EP7-A, NCCLS GP16-T, NCCLS C28-A and FDA draft document "Replacement Reagent and Instrument Family Policy".

L. Test Principle:

PHS reagent is used to measure the Phosphorus concentration by a timed endpoint method. In the reaction, inorganic phosphorus reacts with ammonium molybdate in an acid solution to form a colored phosphomolybdate complex.

The SYNCHRON CX® System(s) automatically proportions the appropriate sample and reagent volumes into a cuvette. The ratio used is one part sample to 67 parts reagent. The system monitors the change in absorbance at 340 nanometers. This change in absorbance is directly proportional to the concentration of phosphorus in the sample and is used by the system to calculate and express the Phosphorus concentration.

Chemical Reaction Scheme



M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-run and total precision studies were designed from NCCLS Guideline EP5-A. The Imprecision Evaluation Criteria (maximum performance limits) for the SYNCHRON Systems PHS Assay appears in the table below.

Imprecision Evaluation Criteria

Precision Measurement	Sample Type	S.D. (mg/dL)	% C.V.	Changeover Value (mg/dL)
Within-Run ^R	Serum/Plasma	0.2	2.0	10.0
Total ^S		0.3	3.0	10.0
Within-Run ^U	Urine	2.0	2.0	100
Total ^I		3.0	3.0	100

Results of the within run and total precision evaluation for SYNCHRON CX and LX Systems are shown in the tables below. The user of a SYNCHRON System should expect the instrument to produce imprecision values less than or equal to the maximum performance limits. Multi-level control materials were used to demonstrate acceptable imprecision within the specifications selected for each sample type.

Precision Summary SYNCHRON CX Systems PHS

Sample	Mean (mg/dL)	S.D. (mg/dL)	% C.V.	N
Within-Run Imprecision				
Serum 1	1.9	0.04	2.2	80
Serum 2	6.4	0.08	1.3	80
Urine 1	40.0	0.54	1.4	80
Urine 2	76.6	1.03	1.3	80
Total Imprecision				
Serum 1	1.9	0.05	2.6	80

Sample	Mean (mg/dL)	S.D. (mg/dL)	% C.V.	N
Within-Run Imprecision				
Serum 1	2.0	0.05	2.4	80
Serum 2	6.6	0.09	1.4	80
Urine 1	41.1	0.43	1.0	80
Urine 2	78.3	0.91	1.2	80
Total Imprecision				
Serum 1	2.0	0.05	2.7	80
Serum 2	6.6	0.10	1.5	80
Urine 1	41.1	0.61	1.5	80
Urine 2	78.3	1.26	1.6	80
Serum 2	6.4	0.11	1.6	80
Urine 1	40.0	0.84	2.1	80
Urine 2	76.6	1.47	1.9	80

Precision Summary SYNCHRON LX System PHS

Precision

b. Linearity/Assay reportable range:

Linearity (analytical range) studies were designed in accordance with NCCLS Guideline EP6-A. The study protocol utilized inter-dilutions of a patient specimen with a zero-level (saline) sample. To achieve an analyte concentration at the high end of the claimed analytical range, the patient specimen for each sample matrix was spiked with phosphate (diabasic). The recovered PHS values were plotted against the expected values an appropriate line fitted by standard linear regression. The table below summarizes the linearity studies.

SYNCHRON System	Sample Type	Measuring Range	Linear Regression Analysis	Assessment
CX PRO	Serum/ Plasma	1.0 – 12.0 mg/dL	$Y = 1.012X - 0.02$	Linear
LX			$Y = 1.016X - 0.08$	Linear
CX PRO	Urine	10-120 mg/dL	$Y = 1.030X - 1.69$	Linear
LX			$Y = 0.995X + 0.28$	Linear

c. Traceability (controls, calibrators, or method):

The SYNCHRON PHS Reagent is designed for use with the SYNCHRON MULTI Calibrator. SYNCHRON MULTI Calibrator (P/N 442600) is sold separate from the reagent kit. SYNCHRON MULTI Calibrator, used in conjunction with SYNCHRON

REAGENTS, is intended for use on SYNCHRON Systems for the calibration of Albumin, Blood Urea Nitrogen (Urea), Calcium, Cholesterol, Creatinine, Glucose, Inorganic Phosphorus, Lactate, Magnesium, Total Protein, Triglycerides, and Uric Acid. The calibrator is prepared from stabilized human serum and is traceable to serum reference material NIST 3139 through the value assignment process.

d. Detection limit:

The claimed sensitivity for inorganic phosphorus determination by the PHS assay is 1.0 mg/dL for serum and 10 mg/dL for urine. The analytical sensitivity of the PHS was evaluated by testing 20 replicates of saline (zero) and a patients sample diluted (with saline) to achieve a concentration less than the claimed sensitivity. Assay sensitivity is distinguishable with 95% confidence if the mean recovery from the sensitivity sample minus two standard deviations is greater than the corresponding mean from the zero sample plus two standard deviations. The results are shown in the tables below.

**Serum Analytical Sensitivity Study
SYNCHRON Systems PHS**

Rep	CX (mg/dL)			LX (mg/dL)		
	Saline	Sample 1	Sample 2	Saline	Sample 1	Sample 2
1	-0.02	0.85	0.69	0.00	0.88	0.71
2	-0.01	0.82	0.75	0.00	0.88	0.71
3	0.00	0.85	0.72	0.00	0.87	0.72
4	0.00	0.87	0.71	0.00	0.87	0.70
5	-0.01	0.85	0.69	0.00	0.87	0.74
6	0.00	0.86	0.70	0.01	0.86	0.67
7	-0.02	0.85	0.70	0.00	0.89	0.69
8	-0.01	0.82	0.71	0.00	0.86	0.73
9	0.00	0.87	0.70	0.00	0.87	0.71
10	0.00	0.88	0.69	0.00	0.87	0.68
11	0.03	0.87	0.72	0.00	0.86	0.72
12	0.00	0.89	0.70	0.00	0.87	0.73
13	-0.01	0.87	0.69	0.00	0.88	0.71
14	-0.01	0.87	0.70	0.00	0.89	0.71
15	-0.01	0.86	0.70	0.00	0.88	0.73
16	0.02	0.85	0.69	0.00	0.87	0.73
17	0.01	0.87	0.72	0.01	0.88	0.68
18	0.00	0.83	0.72	0.00	0.87	0.69
19	0.00	0.87	0.70	0.00	0.88	0.73
20	0.01	0.85	0.71	0.00	0.90	0.71

average	0.00	0.86	0.71	0.00	0.88	0.71
Sd	0.01	0.02	0.01	0.00	0.01	0.02
min	-0.02	0.82	0.69	0.00	0.86	0.67
max	0.03	0.89	0.75	0.01	0.90	0.74
2 SD Limits	0.02	0.82	0.68	0.00	0.85	0.67
	Pass			Pass		

**Urine Analytical Sensitivity Study
SYNCHRON Systems PHS**

Rep	CX (mg/dL)			LX (mg/dL)		
	Saline	Sample 1	Sample 2	Saline	Sample 1	Sample 2
1	0.00	7.6	6.4	0.0	7.8	6.1
2	0.00	7.8	6.5	0.0	7.6	6.4
3	-0.01	7.7	6.5	0.0	7.6	6.3
4	0.1	7.8	6.5	0.0	7.4	7.1
5	0.0	7.9	6.4	0.0	7.8	6.8
6	0.1	7.8	6.8	0.1	7.2	6.1
7	0.0	7.7	6.6	0.0	8.0	6.4
8	0.0	7.8	6.6	0.0	8.3	6.8
9	0.1	7.6	6.7	0.0	7.8	6.5
10	0.1	7.9	6.6	0.1	7.8	6.2
11	0.1	7.8	6.6	0.2	7.8	6.5
12	0.0	7.9	6.5	0.1	7.8	5.9
13	0.1	7.8	6.5	0.0	8.0	6.9
14	0.1	7.7	6.7	0.1	7.3	6.5
15	0.3	7.8	6.5	0.0	7.9	6.7
16	0.1	8.0	6.7	0.0	7.3	6.5
17	0.0	7.8	6.8	0.0	7.8	6.1
18	0.0	8.1	6.9	0.3	7.5	6.4
19	0.1	7.9	6.4	0.0	8.3	6.4
20	0.3	8.1	6.8	0.3	8.1	6.4
average	0.07	7.83	6.60	0.06	7.76	6.45
Sd	0.10	0.14	0.15	0.10	0.31	0.30
min	-0.10	7.60	6.40	0.00	7.20	5.90
max	0.30	8.10	6.90	0.30	8.30	7.10
2 SD Limits	0.27	7.55	6.30	0.26	7.13	5.85
	Pass			Pass		

e. Analytical specificity:

Interference studies were performed on the PHS Reagent to assess common or known substances that could interfere with the method. Interference studies were designed in accordance with NCCLS Guideline EP7-A. A substance was considered to show no significant

interference if the test sample was within 0.4 mg/dL or 4% of the control specimen recovery. The detailed test results are summarized in the table below.

Substance	Source	Level Tested	Observed Effect ^a
Hemoglobin	RBC Hemolysate	250 mg/dL	NSI ^b +0.5 mg/dL
Bilirubin	Porcine	375 mg/dL	NSI
Lipemia	Human	30 mg/dL	NSI
Methotrexate	NA ^c	4+ (visual)	NSI
Cefotaxime	Sodium salt	2.0 mmol/L	NSI
Ascorbic Acid	L-Ascorbic Acid	50 mg/dL	NSI
Fluorescein	Disodium salt	20 mg/dL	+0.7 mg/dL
Nafcillin	NA	75 mg/dL	NSI +0.7 mg/dL
Methylbenzethonium Chloride	NA	5 mg/dL	NSI
Rifampin	NA	10 mg/dL	NSI

^a Plus (+) or minus (-) signs in this column signify positive or negative interference.

^b NSI = No Significant Interference within \pm 0.4 mg/dL or 4%

^c NA = Not applicable

f. Assay cut-off:
Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison experiments were designed using NCCLS Procedure EP9-A, and employed Deming regression analysis to assess the data. The patient correlation studies were obtained using the Beckman Coulter SYNCHRON CX PO4 Assay and the candidate PHS Reagent on representative CX and LX Systems. Patient specimen phosphorus concentrations spanned the analytical range for both sample types.

The tables below summarize the results of the methods comparison studies. The Deming regression analysis demonstrates comparable performance across the analytical range for each sample type between SYNCHRON PHS Reagent and the predicate method.

Serum Method Comparison Summary

Candidate	Platform	Slope	Intercept	r	n	Predicate Method
PHS Reagent	CX	0.997	-0.04	0.998	114	Beckman Coulter SYNCHRON CX Systems PO4 Assay
	LX	0.984	0.12	0.999	112	

Urine Method Comparison Summary

Candidate	Platform	Slope	Intercept	r	n	Predicate Method
PHS Reagent	CX	0.976	0.25	0.996	81	Beckman Coulter SYNCHRON CX Systems PO4 Assay
	LX	1.041	-0.62	0.995	78	

b. Matrix comparison:

Serums versus plasma studies were performed to substantiate the use of EDTA and heparin anticoagulants for phosphorus testing. For each anticoagulant, health volunteers were drawn. Some specimens were spiked with inorganic phosphorus to more adequately cover the claimed performance range. Paired samples (serum and plasma) were analyzed by the PHS assay on both CX and LX Systems. Random sampling of at least 40 patient specimens was analyzed on each platform. Deming regression analysis was used to evaluate the results.

System	Anticoagulant	Level of Anticoagulant Tested	Deming Regression Analysis
SYNCHRON CX	EDTA	1.5 mg/mL	$Y = 0.952X - 0.11$ $r^2 = 0.998$
	Lithium Heparin	14 units/mL	$Y = 1.026X - 0.19$ $r^2 = 0.999$
	Sodium Heparin	14 units/mL	$Y = 1.024X - 0.23$ $r^2 = 0.999$
SYNCHRON LX	EDTA	1.5 mg/mL	$Y = 0.919X + 0.01$ $r^2 = 0.997$
	Lithium Heparin	14 units/mL	$Y = 1.004X - 0.09$ $r^2 = 0.998$
	Sodium Heparin	14 units/mL	$Y = 1.002X - 0.07$ $r^2 = 0.999$

3. Clinical studies:

a. *Clinical sensitivity:*

N/A

b. *Clinical specificity:*

N/A

c. *Other clinical supportive data (when a and b are not applicable):*

N/A

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

The reference interval for the SYNCHRON Systems PHS assay is taken from the predicate insert. Beckman Coulter performed confirmatory studies with the PHS

reagent on CX and LX Systems to verify the claimed reference interval. These confirmatory studies were designed in accordance with NCCLS Guideline C28-A.

Serum samples were drawn from a population of 60 apparently health, non smoking male and female adults (>18 years of age) from Southern California over a three day period. All samples were analyzed in duplicate by the SYNCHRON Systems. A random sampling of 20 subjects was used for the analysis. Acceptance criteria required at least 90% of the sample set to have PHS reported values within the cited reference interval. The results of these studies are consistent with the reference intervals in the reporting results section of the SYNCHRON Systems PHS Reagent Chemistry Information Sheet, and summarized in the chart below.

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
SYNCHRON Systems	Serum or Plasma	2.5 – 4.6 mg/dL	0.81 – 1.49 mmol/L
Literature ⁵	Urine (non-restricted diet)	0.4 – 1.3 g/24 hrs	129 -420 mmol/24 hrs

The labeling recommends that each laboratory should establish its own reference intervals based upon its patient population. The reference intervals listed above were taken from the described study performed on SYNCHRON Systems.

⁵. Tietz, N.W., Clinical Guide to Laboratory Tests, 2nd Edition, W.B. Saunders, Philadelphia, PA (1990).

N. Conclusion:

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