

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

A. 510(k) Number:

k082251

B. Purpose for Submission:

New device

C. Measurand:

Urine Albumin (microalbumin)

D. Type of Test:

Quantitative, turbidimetric method

E. Applicant:

Beckman Coulter, Inc.

F. Proprietary and Established Names:

SYNCHRON[®] Systems Microalbumin (MA) Reagent

G. Regulatory Information:

1. Regulation section:
21 CFR 866.5040

2. Classification:
Class II

3. Product code:
DCF

4. Panel:
Immunology (82)

H. Intended Use:

1. Intended use(s):
See Indication for use below.

2. Indication(s) for use:
MA reagent, when used in conjunction with SYNCHRON CX[®] System(s) and SYNCHRON CX[®] MA Calibrator, is intended for the quantitative determination of albumin (MA) concentration in human urine. Measurement of albumin in urine aids in the diagnosis of kidney dysfunction
3. Special conditions for use statement(s):
For prescription use only
4. Special instrument requirements:
SYNCHRON CX4 system.

I. Device Description:

The SYNCHRON[®] System Microalbumin (MA) Reagent kit consists of the following:

Reagents:

1. Reagent A: Reaction Buffer, in a 33 mL cartridge.
2. Reagent B: MA antibody specific (goat) for human albumin, in a 7.2 mL cartridge.

Calibrators:

SYNCHRON CX Systems MA Calibrator set (previously cleared – k994325) consists of 6 levels of calibrators (Levels 1- 6, 1 x 3 mL bottles), for use on SYNCHRON CX Systems only. MA Calibrator is designed for the generation of a 6-point calibration curve which defines the analytical range for the SYNCHRON Systems MA assay. The calibrator is prepared with pH buffered human serum albumin.

Each serum or plasma donor unit used in the preparation of this material was tested by US FDA approved methods and found to be negative for antibodies to HIV and HCV and nonreactive for HbsAg.

J. Substantial Equivalence Information:

1. Predicate device name(s):
IMMAGE Immunochemistry Systems Microalbumin (MA) Reagent
2. Predicate 510(k) number(s):
K965035

3. Comparison with predicate:

Similarities and Differences between the predicate device and the candidate device:

Attribute	IMMAGE Immunochemistry Systems Microalbumin (MA) Reagent (Predicate device)	SYNCHRON[®] Systems Microalbumin (MA) Reagent (Candidate device)
Intended Use	For the quantitative determination of micro quantities of albumin (MA) in human urine by nephelometry. Measurement of microalbumin in urine aids in the diagnosis of kidney diseases.	For the quantitative determination of of albumin in human urine by turbidimetric method. Measurement of albumin in urine aids in the diagnosis of kidney dysfunction.
Antibodies	Goat anti-human albumin polyclonal Antibodies	Same
Buffer	Phosphate buffer with PEG	Same
Calibration	Use single point adjusted non-linear calibration	Same
Initial measuring range	0.2-4.0 mg/dL	0.2-30 mg/dL
Extended measuring range	4–864 mg/dL	24-97 mg/dL

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

CLSI EP05-A - Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline.

CLSI EP06-A2 - An Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP17-A - Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

CLSI EP07-A2 – Interference testing in Clinical Chemistry; Approved Guideline

EN ISO 17511 - In vitro diagnostic medical devices -- Measurement of quantities in biological samples -- Metrological traceability of values assigned to calibrators and control materials

L. Test Principle:

MA reagent is used to measure the albumin concentration by a turbidimetric method. In the reaction, albumin combines with specific antibody to form insoluble antigen-antibody complexes. The Synchron System(s) automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part sample to 24 parts reagent. The system monitors the change in absorbance at 380

nanometers. This change in absorbance is proportional to the concentration of albumin in the sample and is used by the system to calculate and express albumin concentration based upon a non-linear calibration curve.

M. Performance Characteristics (if/when applicable):

Analytical performance was demonstrated on the CX4 CE system.

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were designed according to the CLSI EP05-A guideline.

Three levels of urine control materials were measured twice a day in duplicates for 20 days (N=80). The results are summarized below:

Synchron CX4:

Sample ID	Mean (mg/dL)	Within-run S.D. (mg/dL)	Total S.D. (mg/dL)	Within-run (CV %)	Total (CV %)
Level 1	0.8	0.08	0.13	9.7	16.3
Level 2	3.0	0.14	0.23	4.5	7.5
Level 3	40.1	0.42	0.59	1.0	1.5

b. *Linearity/assay reportable range:*

The claimed measuring range for the device is 0.2-30mg/dL.

Linearity studies were designed according to the CLSI EP06-A guideline. A high patient urine sample was used to prepare 7 different levels of microalbumin concentration. All samples were measured 4 times on the CX4CE analyzer. Concentration of samples ranged from 0.2 mg/dL to 30 mg/dL (0.2, 0.3, 0.45, 0.6, 1, 3, 6, 12, 18, 24, and 30). An appropriate line was fitted by standard linear regression and the following slope and R² measurements were obtained.

Analyzer	Regression equation for linearity	R ²
CX4CE	y = 1.031x - 0.1482	0.9997

Extended measuring range studies (ORDAC) were performed using 8 concentrations ranging from 20- 100 mg/dL (20, 25, 30, 40, 60, 80 and 100).

The sponsor claimed that the reportable range is 0.2 to 30 mg/dL and the extended range is 24 to 9

Analyzer	Regression equation for ext. linearity	R ²
CX4CE	y = 0.9726x - 1.3438	0.9997

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

The SYNCHRON CX[®] Systems MA Calibrator (six levels) is designed for use on the SYNCHRON CX Systems. Calibrators are traceable to the IFCC

reference preparation for plasma proteins, BCR-470. Traceability process is based on EN ISO 17511. Traceability statements for the calibrator are included in the instructions for use included with the calibrator kit.

Calibrators are stable between +2°C to +8°C until date of expiration. Exposure of Urine Protein Calibrator to temperatures greater than 32°C (90°F) may adversely affect performance. Once opened, the reagent is stable for 60 days unless the expiration date is exceeded. Users are instructed to not freeze the reagent.

d. Detection limit:

Studies on limit of detection were performed according to CLSI EP17 guideline. Limit of blank (LoB) and Limit of detection (LoD) were determined by using saline (0 mg/dL), protein free urine (0 mg/dL), diluted urine protein control (0.2 mg/dL) and diluted urine protein control (0.3 mg/dL). All samples were run in 10 replicates over a period of six days on the CX4CE analyzer. Limit of Blank (LoB) is less than 0.1 mg/dL. The Limit of Detection (LoD) was calculated using the mean and SD for the low sample measurements:

$$\text{LoD} = \text{LoB} + 1.653 * \text{SD}$$

The Limit of Detection (LoD) is less than 0.2 mg/dL.

e. Analytical specificity:

Interference studies were designed according to the CLSI EP7-A2 guideline. Three levels of patient samples or pools were spiked with the known interference substances and analyzed on the Synchron CX 4 CE analyzer. No significant interference was defined as the observed value for Microalbumin values ≤ 2.3 mg/dL is $\leq \pm 0.25$ mg/dL and values > 2.3 mg/dL is $< 10.8\%$ difference of the expected value (neat sample). The sponsor claimed that there was no significant interference ($< 10.8\%$ or $\leq \pm 0.25$ mg/dL) by the following interferents:

- Ascorbic acid to 500 mg/dL
- Calcium up to 130 mg/dL
- Citrate up to 50 mg/dL
- Creatinine up to 160 mg/dL
- Glucose up to 200 mg/dL
- Magnesium up to 400 mg/dL
- Oxalate up to 30 mg/dL
- Urea up to 140 mg/dL

The sponsor has the following limitations in the labeling:

- Do not use turbid samples. Samples should be centrifuged before testing if they have debris in them.

- Do not use samples contaminated with blood.
- If serum proteins carryover is suspected, a saline sample should be assayed prior to assaying the patient samples.

f. Assay cut-off:
Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed based on the CLSI EP9-A guideline. A total of 111 urine samples were evaluated using Synchron CX4 (candidate) and IMMAGE (predicate). Deming regression analyses were used to evaluate the correlations between results. Correlation regression is summarized below:

$$Y = 0.990X - 0.11, r = 0.987, \text{ range of sample tested} = 0.2\text{-}27 \text{ mg/dL}$$

(X= IMMAGE and Y= Synchron CX4)

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:

Reference intervals were taken from the literature:

*Reference: American Diabetes Association Position statement on Diabetic Neuropathy - Diabetes Care (20): S24 – S27.

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.