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

A. 510(k) Number:

k091846

B. Purpose for Submission:
New Device

C. Measurand:
α - Amylase

D. Type of Test:
Quantitative, enzymatic

E. Applicant:
Beckman Coulter, Inc.

F. Proprietary and Established Names:
Synchron Systems G7 Amylase (AMY7) Reagent

G. Regulatory Information:

1. Regulation section:
   21 CFR § 862.1070 - Amylase test system
2. Classification:
   Class II – reagent
3. Product code:
   JFJ – Catalytic Methods, Amylase
4. Panel:
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):
   Refer to Indications for Use below.
2. Indication(s) for use:
   AMY7 reagent, in conjunction with SYNCHRON® System(s), UniCel® DxC System(s) is intended for the quantitative determination of total Amylase activity in human serum, plasma or urine.

   Amylase measurements are used primarily in the diagnosis and treatment of pancreatitis.
3. Special conditions for use statement(s):
   Prescription use only
4. Special instrument requirements:
   SYNCHRON CX 7 PRO system and UniCel DxC 600 system.

I. Device Description:

The AMY7 reagent is supplied as a liquid, ready-to-use, reagent kit.
Reactive ingredients include: α-glucosidase (microorganism) (9700 U/L), 4,6-ethylidene(G1)-4-nitrophenyl (G7)-α-(1→4)-D-maltoheptaoside (Ethyledene

Protected Substrate = EPS) (11 mmol/L), Sodium Chloride (87 mmol/L), Calcium Chloride (0.08 mmol/L), Magnesium Chloride (12.6 mmol/L), non-reactive chemicals and, and preservative.

AMY7 reagent is used to measure the amylase activity by an enzymatic rate method. The system monitors the change in absorbance at 410 nanometers. This change in absorbance is directly proportional to the activity of AMY7 in the sample and is used by the System to calculate and express the total AMY7 activity.
The SYNCHRON G7 Amylase (AMY7) Reagent is designed for performance on the SYNCHRON LX®, UniCel® DxC 600/800, and SYNCHRON CX® PRO Clinical Systems. The reagent kit contains two 200-test cartridges

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Thermo Fisher Amylase EPS Reagent
2. Predicate 510(k) number(s):
   k070064
3. Comparison with predicate:

	Candidate device Synchron Systems G 7 Amylase (AMY7) Reagent	Predicate Thermo Fisher Amylase EPS Reagent (k070064)
Analyte	α-Amylase	α-Amylase
Method	Enzymatic rate; EPS substrate	Enzymatic rate; EPS substrate
Reagent volume	Two part liquid: Reagent A: 175 ul Reagent B: 35 ul	Two-part liquid Reagent A: 175 ul Reagent B: 35 ul
Format	Liquid	Liquid
Open reagent (on-board) stability	21 days	35 days
Traceability	Traceable to IFCC Amylase EPS reference method	Traceable to IFCC Amylase EPS reference method
Sample matrix	Plasma, serum, urine	Plasma, serum, urine

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

CLSI EP-5A2; *Evaluation of Precision Performance of Clinical Chemistry Devices*
CLSI EP-6A; *Evaluation of the Linearity of Quantitative Analytical Methods*
CLSI EP-17A; *Protocols for Demonstration, Verification, and Evaluation of Limits of Detection and Quantitation*
CLSI EP-7A2; *Interference Testing in Clinical Chemistry*
CLSI EP-9A2; *Method Comparison and Bias Estimation Using Patient Samples*

CLSI C-28A2; *How to Define and Determine Reference Intervals in the Clinical Laboratory*

L. Test Principle:

AMY7 reagent is used to measure amylase activity by an enzymatic rate method.2 In the reaction, amylase cleaves 4,6-ethylidene(G1)-4-nitrophenyl(G7)-α-(1→4)-D-maltoheptaoside (Ethyledene Protected Substrate = EPS) and subsequent hydrolysis of all the degradation products to p-nitrophenol with the aid of α -glucosidase.
The SYNCHRON CX® System(s) automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part sample to 30 parts reagent. The system monitors the change in absorbance at 410 nanometers.
This change in absorbance is directly proportional to the activity of AMY7 in the sample and is used by the System to calculate and express the total AMY7 activity.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

Within-run and total imprecision studies were designed from CLSI Guideline EP5-A2. The experimental design utilizes duplicate sample analysis, twice daily, over twenty working days.Multi-level controls, serum and urine pools were used to demonstrate acceptable imprecision for each analyte. Results were compiled for one instrument, for twenty days, at two runs per day and two observations per run. Data analysis employs analysis of variance for within-run and total imprecision estimates. Results for the within-run and total imprecision studies for SYNCHRON Systems G7 Amylase (AMY7) Reagent are shown in Tables below. All results pass the evaluation criteria listed criteria listed in the imprecision evaluation criteria table.

Precision Study Results on SYNCHRON CX7 PRO Clinical System

Sample	Mean (U/L)	S.D. (U/L)	%C.V.	N
Within-Run Imprecision				
Serum/Plasma Level 1	75.8	1.3	1.7	80
Serum/Plasma Level 2	899.5	4.7	0.5	80
Serum/Plasma (ORDAC)	1762.0	12.9	0.7	80
Urine	54.9	1.3	2.4	80
Urine	164.6	1.7	1.1	80
Urine (ORDAC)	1182.9	11.8	1.0	80
Total Imprecision				
Serum/Plasma Level 1	75.8	1.4	1.8	80
Serum/Plasma Level 2	899.5	8.2	0.9	80
Serum/Plasma (ORDAC)	1762.0	34.9	2.0	80
Urine	54.9	1.4	2.5	80
Urine	164.6	1.9	1.2	80
Urine (ORDAC)	1182.9	60.4	5.1	80

Precision Study Results on UniCel DxC 600 SYNCHRON Clinical System

Sample	Mean (U/L)	S.D. (U/L)	%C.V.	N
Within-Run Imprecision				
Serum/Plasma Level 1	78.7	1.0	1.3	80
Serum/Plasma Level 2	913.6	4.5	0.5	80
Serum/Plasma (ORDAC)	1775.4	8.7	0.5	80
Urine	56.5	0.7	1.2	80
Urine	168.4	0.9	0.5	80
Urine (ORDAC)	1181.0	6.0	0.5	80
Total Imprecision				
Serum/Plasma Level 1	78.7	0.8	1.1	80
Serum/Plasma Level 2	913.6	5.5	0.6	80
Serum/Plasma (ORDAC)	1775.4	11.0	0.6	80
Urine	56.5	0.7	1.2	80
Urine	168.4	1.1	0.7	80
Urine (ORDAC)	1181.0	55.5	4.7	80

b. Linearity/assay reportable range:

Linearity (analytical range) studies were designed in accordance with CLSI Guideline EP6-A. *"Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach."* The experimental design involved multiple replicates (4) over several amylase activity levels (7), as directed by the guideline. A serum pool obtained from a local Blood Bank was used for the linearity study. The experimental design involved multiple replicates (4) over several amylase activity levels (7), as directed by the guideline. A low Amylase level serum pool was prepared by diluting an aliquot of the serum pool with saline to achieve the target low concentration. A high Amylase level serum pool was prepared by spiking an aliquot of the serum pool with a spiking solution to achieve the target high concentration. A low Amylase level urine pool was prepared by diluting an aliquot of the urine pool with deionized (D.I.) water to achieve the target low concentration. A high Amylase level urine pool was prepared by spiking an aliquot of the urine pool with a spiking solution to achieve the target high concentration. Inter-dilutions of the low and high pools were done to prepare the seven level linearity set (serum and urine) for the study. The recovered Amylase values were plotted against the expected values and an appropriate line fitted by standard linear regression.

Additional extended linearity study:
ORDAC (Over Range Detection and Correction) allows the extension of the usable range by using a predetermined dilution ratio for those samples which exceed the usable range of the chemistry. The recovered amylase values were plotted against the expected values and an appropriate line fitted by standard linear regression. Evaluation criteria assess the goodness of fit of the line, ensuring that no points deviate outside the imprecision of the assay. Tables below summarize the results of the linearity studies.

SYNCHRON System	Sample Type	Measuring Range	Linear Regression Analysis	Assessment
CX7 PRO	Serum/ Plasma	8 – 1200 U/L 1000-2000 U/L (ORDAC)	$Y = 0.9940X + 6.9165$ $R^2 = 0.9997$	Linear
	Urine	8 – 1200 U/L 1000-2000 U/L (ORDAC)	$Y = 1.0010X – 3.8530$ $R^2 = 0.9998$	Linear
DxC 600	Serum/ Plasma	5 – 1200 U/L 1000-2000 U/L (ORDAC)	$Y = 0.9980X + 8.1073$ $R^2 = 0.9998$	Linear
	Urine	5 – 1200 U/L 1000-2000 U/L (ORDAC)	$Y = 1.0012X – 2.4899$ $R^2 = 0.9999$	Linear

The results of the study support the sponsor's claimed range and the assay is linear from 8-1200 U/L for serum and urine on the SYNCHRON CX7 PRO system and 5-1200 U/L for serum and urine on the UniCel DxC 6000 system. For the extended linearity (ORDAC) range, the assay is linear from 1000-2000 U/L for both serum and urine on both SYNCHRON CX7 PRO and UniCel DxC 600 systems.

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

The sponsor stated that calibration is not required, since the SYNCHRON instrument systems calculate U/L of activity by multiplying the measured rate of reaction by a programmed calculation factor, which has been derived to provide traceability to the International Federation of Clinical Chemistry (IFCC) Amylase reference measurement procedure.

The stability protocols were designed according to Beckman Product Development Procedures, which assess materials at time zero and various time/temperature intervals to determine product dating. The stability data supports a shelf-life dating claim of 18 months for the AMY7 Reagent.

Reagent Open Cartridge Stability

On board reagent stability claims are validated by control recovery experiments. For the SYNCHRON Systems G7 Amylase (AMY7) Reagent, the onboard stability claim is 21 days.

d. Detection limit:

Per CLSI EP17-A: "Protocols for Determination of Limits of Detection and Limits of Quantitation: Approved Guideline", Beckman Coulter uses the term Analytical Sensitivity to characterize Limit of Detection in its product labeling. The sponsor defined analytical sensitivity as the lowest measurable concentration which can be distinguished from zero with 95% confidence. The analytical sensitivity of the AMY7 assay was evaluated by testing 20 replicates of saline (zero) and a patient sample diluted (with saline for serum samples and deionized water for urine samples) to achieve a concentration less than the claimed sensitivity. Target amylase concentration was 80% of the low end analytical range claim (5 U/L for LX/DxC and 8 U/L for CX PRO). Testing was performed on UniCel DxC 600 and SYNCHRON CX7 PRO Clinical Systems.

The sponsor determined that the analytical sensitivity of the AMY7 assay is 8 U/L on SYNCHRON CX PRO 7 system and 5 U/L on UniCel DxC 600 system.

e. Analytical specificity:

Interference studies were designed from CLSI Guideline EP7-A: *"Interference Testing in Clinical Chemistry – Approved Guideline"* and used to assess common or known substances which could interfere with the SYNCHRON Systems G7 Amylase (AMY7) method. Three sample pools

(which represent low, mid, and high analyte levels) were tested at different levels of Bilirubin, Hemoglobin, and Lipemia (Human and Intralipid) to determine the magnitude of the effect. Only one analyte level was tested for human lipemia so as not to alter the human lipemia sample; there is no commercially available spiking solution for human lipemia. Each sample was tested in two cups, two replicates per cup, to give a total of four replicates per sample on UniCel DxC 600 and SYNCHRON CX PRO 7 systems.
The data analysis involved calculating the difference in recovery of the samples with and without the potential interferent in accordance with the CLSI Procedure EP7-A.
The criteria for determining interference are indicated in Table 1. The recovery bias must not exceed 2 times the within run precision claim SD or %CV for AMY7 (6 U/L SD or 7.0% CV).

Table 1. SYNCHRON Systems G7 Amylase (AMY7) Reagent Evaluation Criteria

Analyte	**Sample Type**	**SD (U/L)**	**%CV Specification**	**Crossover**	**Units**
AMY7	Serum	3.0	3.5	85.7	U/L

Data from the sponsor's interference studies are summarized in Tables below:

SYNCHRON CX 7 and SYNCHRON DxC 600 Serum Interferences Summary

Substance	**Source**	**Level Tested**	**Observed Effect on Analyte[a]**
Bilirubin (unconjugated)	Bovine	30 mg/dL	NSI[a]
Bilirubin (conjugated)	Bovine	30 mg/dL	NSI[a]
Hemoglobin	RBC hemolysate	375 mg/dL	NSI[a]
Lipemia	Intralipid[b]	500 mg/dL	NSI[a]
	Human	Serum Index 11	NSI[a]
Ascobic Acid	NA[c]	200mg/dL	NSI
Glucose	NA[c]	2000mg/dL	NSI

[a] NSI = No Significant Interference (within ± 6.0 U/L or 7%).
[b] Intralipid is a registered trademark of KabiVitrum, Inc., Clayton, NC 27250
[c] NA= Not applicable

f. Assay cut-off:

Not Applicable

2. <u>Comparison studies:</u>

a. Method comparison with predicate device:

Method comparison experiments were designed using CLSI Procedure EP9-A2: "*Method Comparison and Bias Estimation Using Patients Samples*" and employed Deming regression analysis to assess the data. The patient correlation studies were obtained using the predicate Reagent and the candidate AMY7 Reagent on representative UniCel DxC 600 and SYNCHRON CX PRO 7 systems. Patient specimen Amylase concentrations spanned the analytical range for both (serum and urine) sample types. To cover both the high and low ends of the analytical range, some specimens were spiked with spiking material (516,000 U/L Amylase solutions), while others were diluted with saline (serum samples) and DI water (urine samples).

Tables below summarize the results of the methods comparison studies. The Deming regression analysis demonstrates comparable performance across the analytic range for each sample type between SYNCHRON AMY7 Reagent and the predicate method.

Serum Method Comparison Summary

Candidate	**Platform**	**Slope**	**Intercept**	**R**	**N**	**Predicate Method**
G7 Amylase (AMY7) Reagent	CX7 PRO	1.150	-4.089	0.9999	87	Thermo Fisher Amylase EPS - G7 Reagent
	DxC 600	1.082	-3.369	0.9999	83	

Urine Method Comparison Summary

Candidate	**Platform**	**Slope**	**Intercept**	**R**	**N**	**Predicate Method**
G7 Amylase (AMY7) Reagent	CX7 PRO	1.109	-2.086	0.9997	78	Thermo Fisher Amylase EPS –G7 Reagent
	DxC 600	1.039	-0.703	0.9997	78	

Additional different platforms studies:

To demonstrate equivalent performance between the SYNCHRON CX PRO and SYNCHRON LX/UniCel DxC Clinical Systems, results from method comparison studies for both serum and urine sample types from CX7 PRO System were plotted against results from the DxC 600 System. The linear regression equation for the serum type is: Y = 0.998X – 0.315, R= 0.9999, N=83. The linear regression equation for the urine type is: Y = 0.996X – 0.263, R = 0.9994, N=78. (X=SYNCHRON CX7 PRO, Y=UniCel DxC 600)

b. Matrix comparison:

The objective of this testing is to evaluate the effect of anticoagulants (Sodium Heparin and Lithium Heparin) in primary blood collection tubes on the recovery of Amylase using the SYNCHRON Systems G7 Amylase (AMY7) reagent and to support plasma as a claimed sample type. For each anticoagulant, plasma and serum samples from apparently healthy volunteers were drawn. Low serum samples were prepared by diluting serum samples with saline. High serum samples were prepared by spiking serum samples with spiking solution to achieve high concentration.
The plasma recoveries were compared to the corresponding serum recoveries for the same donor. Paired samples (serum and plasma) were analyzed by the AMY7 assay on representative UniCel DxC 600 and SYNCHRON CX PRO 7 systems. Deming regression analysis was used to evaluate the results. Table below summarizes the results.

System	Anticoagulant	Deming Regression Analysis
SYNCHRON CX7 PRO	Lithium Heparin	Y = 1.004 X + 0.62; r = 1.000
	Sodium Heparin	Y = 1.002 X + 0.69; r = 1.000
UniCel DxC 600	Lithium Heparin	Y = 0.996 X + 1.21; r = 1.000
	Sodium Heparin	Y = 1.000 X + 0.85; r = 1.000

Sodium heparin and lithium heparin anticoagulants are acceptable anticoagulants to be used.

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):

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:
The sponsor performed confirmatory studies with the AMY7 reagent on SYNCHRON CX7 PRO and UniCel DxC 600 SYNCHRON Clinical Systems to verify the literature reference interval. These confirmatory studies were designed in accordance with CLSI Guidance C28-A2.
Serum samples were collected from a population of 20 apparently healthy, non-smoking adults (> 18 years of age) from Southern California over a three-day

period. Urine samples were collected from a population of 40 apparently healthy, non-smoking, 20 male and 20 female adults (> 18 years of age) from Southern California over a two-day period. All samples were analyzed in duplicate by the SYNCHRON CX7 PRO and UniCel DxC 600 System. A random sampling of 20 subjects was used for the analysis of each reference interval.

The results of these studies are consistent with the reference intervals in the REPORTING RESULTS section of the SYNCHRON Systems AMY7 Reagent Chemistry Information Sheets and summarized in Table below.

AMY7 Reference Interval Summary

Sample Type	SYNCHRON System	REFERENCE INTERVAL
Serum or Plasma	CX PRO	28 – 100 U/L
	LX/DxC	28 – 100 U/L
Urine	CX PRO	21 – 447 U/L (Female)
		16 – 491 U/L (Male)
	LX/DxC	21 – 447 U/L (Female)
		16 – 491 U/L (Male)

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.