

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

A. 510(k) Number:

k070064

B. Purpose for Submission:

New Device

C. Measurand:

α - Amylase

D. Type of Test:

Quantitative, enzymatic

E. Applicant:

Thermo Fisher Scientific, Inc.

F. Proprietary and Established Names:

Amylase EPS 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.

2. Indication(s) for use:

The Amylase EPS reagent is used for the quantitative determination of α -Amylase (1,4- α -D-glucan glucanohydrolase EC3.2.1.1) in human serum, plasma or urine on Beckman Coulter SYNCHRON CX[®]/LX[®] Systems.

α -Amylase is most frequently measured in the diagnosis of acute pancreatitis, when serum levels may be grossly elevated.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

Beckman Coulter SYNCHRON CX[®]/LX[®] Systems.

I. Device Description:

The Amylase EPS reagent is supplied as a liquid, ready-to-use, two reagent kit. Reagent A contains α -glucosidase (≥ 9700 U/L), NaCl (87 mmol/L), MgCl₂ (12.6 mmol/L), CaCl₂ (0.08 mmol/L), preservative, and buffer (53.3 mmol/L) pH 7.2 +/-

0.05 at 20°C. Reagent B contains EPS (22 mmol/L), buffer (54.4 mmol/L), and preservative. The reagent A is supplied in 2X40 mL and B in 2X8.5 mL containers.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Roche COBAS Ready Amylase reagent
2. Predicate 510(k) number(s):
k903309
3. Comparison with predicate:

Item	Device Amylase EPS reagent	Predicate Roche COBAS Ready Amylase reagent
Analyte	α -Amylase	α -Amylase
Method	Enzymatic rate; EPS substrate	Enzymatic rate; EPS substrate
Reagent components	Two part liquid: Reagent A: α -glucosidase (\geq 9700 U/L), NaCl (87 mmol/L), MgCl ₂ (12.6 mmol/L), CaCl ₂ (0.08 mmol/L), preservative, buffer (53.3 mmol/L) pH 7.2 \pm 0.05 at 20°C. Reagent B: EPS (22 mmol/L), buffer (54.4 mmol/L), and preservative.	Two-part liquid Reagent 1: α -glucosidase (\geq 4000 U/L), NaCl (87 mmol/L), MgCl ₂ (12.6 mmol/L), CaCl ₂ (0.075 mmol/L), preservative, HEPES buffer (52.5 mmol/L) pH 7.0 at 37°C. Reagent 2: EPS (22 mmol/L), HEPES buffer (52.5 mmol/L), and preservative.
Format	Liquid	Liquid
Linearity/Assay range	4-1800 U/L on SYNCHRON CX9 4-2000 U/L on SYNCHRON LX20	3-1500 U/L
Low limit of Detection	4 U/L	3 U/L
Closed reagent stability	Until the expiration date when stored at 2-8°C	Until the expiration date when stored at 2-8°C
Open reagent (on-board) stability	35 days	28 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; Approved Guideline

CLSI EP-6A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

L. Test Principle:

The oligosaccharide substrate 4,6-ethylidene-(G7)-p-nitrophenyl-(G1)- α -D-maltoheptaoside (EPS-G7) is cleaved by α -amylase into various smaller fragments. These fragments are further hydrolyzed in a second step by α -glucosidase producing glucose and p-nitrophenoxide (pNP). The rate of pNP formation is proportional to the pancreatic α -amylase activity in the sample and is measured by the rate of increase in absorbance.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

Precision was evaluated following recommendations in CLSI EP-5A2. Studies were conducted at one site over 20-day period with 2 runs per day (total of 40 runs). Three commercially available controls were used for serum and two for urine. Precision was evaluated for both SYNCHRON LX20 and CX9 instruments.

Within-run Precision for serum

	Description	Control 1	Control 2	Control 3
Beckman Coulter SYNCHRON LX20	Number of data points	80	80	80
	Mean (U/L)	68.5	288.5	799.8
	SD (U/L)	1.5	2.6	9.9
	CV (%)	2.2	0.9	1.2
Beckman Coulter SYNCHRON CX9	Number of data points	80	80	80
	Mean (U/L)	70.3	284.5	810.2
	SD (U/L)	1.8	3.3	4.8
	CV (%)	2.6	1.2	0.6

Day-to-day Precision for serum

	Description	Control 1	Control 2	Control 3
Beckman Coulter SYNCHRON LX20	Number of data points	80	80	80
	Mean (U/L)	68.5	288.5	799.8
	SD (U/L)	1.5	3.8	9.9
	CV (%)	2.3	1.3	1.2
Beckman Coulter SYNCHRON CX9	Number of data points	80	80	80
	Mean (U/L)	70.3	284.5	810.2
	SD (U/L)	2.3	4.1	7.8
	CV (%)	3.3	1.4	1.0

Within-run Precision for urine

	Description	Control 1	Control 2
Beckman Coulter SYNCHRON LX20	Number of data points	80	80
	Mean (U/L)	52.7	154.7
	SD (U/L)	1.7	1.7
	CV (%)	3.2	1.1
Beckman Coulter SYNCHRON CX9	Number of data points	80	80
	Mean (U/L)	54.0	156.9
	SD (U/L)	2.5	2.1
	CV (%)	4.6	1.4

Day-to-day Precision for urine

	Description	Control 1	Control 2
Beckman Coulter SYNCHRON LX20	Number of data points	80	80
	Mean (U/L)	52.7	154.7
	SD (U/L)	1.9	3.2
	CV (%)	3.5	2.1
Beckman Coulter SYNCHRON CX9	Number of data points	80	80
	Mean (U/L)	54.0	156.9
	SD (U/L)	2.8	2.9
	CV (%)	5.2	1.9

b. Linearity/assay reportable range:

To evaluate linearity and reportable range, the sponsor followed CLSI EP-6A. Linearity studies were performed on Beckman Coulter SYNCHRON LX20 and CX9 analyzers. Two patient sample pools (high and low) were used to prepare 10-12 concentration levels for an approximate range of 0 – 2200 U/L. Each test level was run in triplicate on the above analyzers. A linear regression analysis was conducted for measured and assigned values with established acceptance criteria of measured values being within 95-105% of the assigned value. The same protocol was used for linearity analysis for serum, plasma, and urine. The results indicated that EPS reagent is linear up to 2000 U/L for LX20 and 1800 U/L for CX9 analyzers. The same linearity claims were reported for all sample types. The sponsor has claimed the assay reportable range tabulated below for specific instrument and sample types.

	Serum	Plasma	Urine
Reportable range	LX: 4 – 2000 U/L CX: 4 – 1800 U/L	LX: 4 – 2000 U/L CX: 4 – 1800 U/L	LX: 4 – 2000 U/L CX: 4 – 1800 U/L

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

Calibrator. The sponsor states that user calibration is not required since the SYNCHRON instrument system calculates U/L of activity by multiplying the measured rate of reaction by the programmed Calculation Factor. This Calculation Factor has been derived to provide traceability to the IFCC Amylase reference measurement procedure.

Controls. To ensure adequate quality control, the sponsor recommends running two quality controls, normal and abnormal, along with the samples. The control materials are not provided.

The sponsor conducted on-board stability studies using Amylase EPS reagent after accelerated storage equivalent to 21 months. The sponsor reported that all tests recovered within +/- 5%. On-board stability was claimed as 35 days.

d. Detection limit:

To demonstrate the lower limit of detection, a serum matrix equivalent solution (Serasub) containing no amylase was assayed 12 times. The sponsor defined the limit of detection as the lowest measurable analyte level that can be significantly distinguished from zero, which was calculated as the mean value of zero-concentration (blank) sample $\pm 2SD$. This value of the blank sample was demonstrated to be 4.0 U/L for SYNCHRON LX20 and 4.1 U/L (Mean = 0.42; SD = 1.83) for SYNCHRON CX9. Based on these results, the sponsor claimed LOD of 4.0 U/L.

e. Analytical specificity:

The sponsor evaluated the effect of hemoglobin (0-1000 mg/dL), unconjugated bilirubin (0 – 90 mg/dL) and conjugated bilirubin (0-60 mg/dL), lipemia (intralipid) (0-2000 mg/dL), glucose (0 – 120 mmol/L), and ascorbic acid (0 – 200 mg/dL) on normal serum controls spiked with the interferents, and then compared with unspiked control. Based on the sponsor-defined interference limit of $\pm 10\%$ of control, following interference limit claims were set by the sponsor for two instruments tested.

Interferent	No Interference claim up to (mg/dL)	
	SYNCHRON LX20	SYNCHRON CX9
Hemoglobin	900	1000
Lipemia	2000	1000
Unconjugated bilirubin	60	60
Conjugated Bilirubin	60	60
Ascorbic acid	200	200
Glucose	2160	2160

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Performance of the Amylase EPS Reagent on Beckman Coulter SYNCHRON LX20 and SYNCHRON CX9 was compared with performance of the predicate device, Roche Amylase Reagent (k903309), on the Hitachi 917 chemistry analyzer. A summary of the sample number, composition, and the results of linear regression analysis is given below.

	Serum/Plasma	Serum only	Plasma only	Urine
Total number of pairs	111	70	41	LX: 106 CX: 99
Range of results (U/L)	45 – 1864	45 – 1864	45 – 1864	45 – 1864
Slope	LX: 0.975 CX: 0.972	LX: 0.973 CX: 0.970	LX: 0.979 CX: 0.975	LX: 1.027 CX: 1.065
Intercept	LX: -3.7 CX: -3.2	LX: -3.0 CX: -1.5	LX: -4.8 CX: -6.1	LX: -7.6 CX: -4.1
R	LX: 0.9994 CX: 0.9991	LX: 0.9994 CX: 0.9993	LX: 0.9995 CX: 0.9987	LX: 0.9992 CX: 0.9975

b. Matrix comparison:

To demonstrate comparable performance between serum and lithium-heparin or sodium-heparin plasma, the sponsor compared 10 paired serum and plasma samples on SYNCHRON LX20 and CX9 analyzers using Amylase EPS reagent. Compared with the sera for the sample values ranged (33 – 101 U/L), the mean recovery for the lithium-heparin was 98.6% (LX20) and 97.8 (CX9); and for sodium-heparin plasma it was 99.0% (LX20) and 98.0 (CX9). The sponsor conducted method comparison studies separately for each matrix as well (see above).

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 expected values of Amylase were based on literature*.

Serum/Plasma: 28 – 100 U/L (at 37°C)

Urine – Male: 16 – 491 U/L (at 37°C)

Urine – Female: 58 – 283 U/L (at 37°C)

* Junge, W. et. al. Development of assays for the determination of total and pancreatic amylase at 37C according to the principle recommended by the IFCC: Clin. Biochem. 2001: 34:607–15.

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.