

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

A. 510(k) Number:

k101090

B. Purpose for Submission:

Alkaline Phosphatase: Addition of plasma to the cleared device (k080874)

Aspartate Aminotransferase: Addition of plasma to the cleared device (k080874)

Amylase: Addition of plasma to the cleared device (k080823)

C. Measurand:

Alkaline Phosphatase, Aspartate Aminotransferase and Amylase.

D. Type of Test:

Quantitative colorimetric chemistry tests

E. Applicant:

Medica Corporation

F. Proprietary and Established Names:

EasyRA Alkaline Phosphatase Reagent

EasyRA Aspartate Aminotransferase Reagent

EasyRA Amylase Reagent

G. Regulatory Information:

Device Classification Name	Device Classification	Regulation Number	Product Code	Panel
Alkaline phosphatase or isoenzymes test system	Class II	21 CFR § 862.1050	CJE	Clinical Chemistry (75)
Aspartate amino transferase (AST/SGOT) test system	Class II	21 CFR § 862.1100	CIT	Clinical Chemistry (75)
Amylase test system	Class II	21 CFR § 862.1070	JFJ	Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indication(s) for use below.

2. Indication(s) for use:

The EasyRA Alkaline phosphatase (ALP) reagent is intended for the quantitative determination of alkaline phosphatase in human serum and plasma, using the MEDICA “EasyRA Chemistry Analyzer” in clinical laboratories. Measurement of alkaline phosphatase or its isoenzymes are used in the diagnosis and treatment of liver, bone, parathyroid and intestinal diseases. For *in vitro* diagnostic use only.

The EasyRA Aspartate Aminotransferase (AST) reagent is intended for the quantitative determination of the enzyme Aspartate Aminotransferase in human serum and plasma, using the MEDICA “EasyRA Chemistry Analyzer” in clinical laboratories. Measurement of alkaline phosphatase measurements are used in the diagnosis and treatment of certain types of liver and heart diseases. For *in vitro* diagnostic use only.

The EasyRA Amylase (AMY) reagent is intended for the quantitative determination of amylase in human serum and plasma, using the MEDICA “EasyRA Chemistry Analyzer” in clinical laboratories. a-Amylase in serum/plasma is used for the diagnosis and treatment of pancreatitis (inflammation of the pancreas) and other pancreatic disorders.

3. Special conditions for use statement(s):
This device is intended for professional use only.
4. Special instrument requirements:
For use on the Medica EasyRA Chemistry analyzer.

I. Device Description:

The EasyRA Alkaline phosphatase Reagent (ALP) is provided in four ready-to-use plastic wedges, each containing 27 mL of ALP Buffer Reagent (R1) and 6 ml of ALP Substrate Reagent (R2). R1 reagent consists of HEDTA buffer with 2-Amino-2-methyl-1-propanol, Magnesium Chloride and Zinc Sulfate. R2 reagent is comprised of 4-Nitrophenyl Phosphate.

The EasyRA Aspartate Aminotransferase (AST) Reagent is provided in four ready-to-use plastic wedges, each containing 31 mL of AST Buffer Reagent (R1) and 7 ml of AST Substrate Reagent (R2). R1 reagent consists of Tris buffer with L-Aspartate, rabbit muscle LDH and porcine muscle MDH enzymes. R2 reagent is comprised of α -Ketoglutarate and NADH.

The EasyRA Amylase (AMY) Reagent is provided in four ready-to-use plastic wedges, each containing 39 mL of reagent. The reagent consists of a MES buffer with 2-chloro-4-nitrophenol- α -D-maltotrioxide, sodium chloride, calcium acetate, potassium thiocyanate, and sodium azide.

J. Substantial Equivalence Information:

Predicate device name	Predicate 510(k) number
EasyRA Alkaline phosphatase Reagent	k080874

EasyRA Aspartate Aminotranferase Reagent	k080874
EasyRA Amylase Reagent	k080823

Comparison with predicate:

EasyRA Alkaline phosphatase Reagent Similarities and Differences		
Item	Device	Predicate (k080874)
Intended Use/Indications for Use	Same	The quantitative determination of alkaline phosphatase. Measurement of alkaline phosphatase or its isoenzymes are used in the diagnosis and treatment of liver, bone, parathyroid and intestinal diseases.
Sample	Serum, Plasma	Serum
Measuring Range	Same	7 – 800 U/L
Test Principle	Same	The formation of 4-nitrophenol, which results from the Alkaline Phosphatase hydrolysis of 4-nitrophenyl phosphate substrate, changes the sample absorbance at 405 nanometers.
Format	Same	Liquid ready-for-use
Analyzer	Same	MEDICA “EasyRA Chemistry Analyzer”

EasyRA Aspartate Aminotranferase Reagent Similarities and Differences		
Item	Device	Predicate (k080874)
Intended Use/ Indications for Use	Same	A quantitative measurement of Aspartate Aminotranferase. Measurement of aspartate aminotranferase measurements are used in the diagnosis and treatment of certain types of liver and heart diseases.
Sample	Serum, Plasma	Serum
Measuring Range	Same	5.5 – 400 U/L
Test Principle	Same	The Aspartate Aminotranferase (AST) enzyme catalyzes the transfer of the Aspartate amino group to α -Ketoglutarate (α -KG) with the formation of L-glutamate and oxaloacetate (OAA). The OAA is then reduced to L-malate by reacting with NADH in a reaction catalyzed by malate dehydrogenase (MDH). The amount of NADH that is oxidized to NAD reduces the sample absorbance at 340 nm. This decrease is directly proportional to the activity of AST in serum.
Format	Same	Liquid ready-for-use
Analyzer	Same	MEDICA “EasyRA Chemistry Analyzer”

EasyRA Amylase Reagent Similarities and Differences		
Item	Device	Predicate (k080823)
Intended Use/ Indications for Use	Same	A quantitative measurement of α -Amylase. Amylase measurements are used for the diagnosis and treatment of pancreatitis (inflammation of the pancreas) and other pancreatic disorders.
Sample	Serum, Plasma	Serum
Measuring Range	Same	2 – 1200 U/L
Test Principle	Same	The α -Amylase (AMY) enzyme hydrolyses the chromogenic substrate, 2-chloro-4-nitrophenol- α -D-maltotrioxide to form 2-Chloro-4-nitrophenol, which can be detected spectrophotometrically at 405 nm to give a direct measurement of α -amylase activity in the sample.
Format	Same	Liquid ready-for-use
Analyzer	Same	MEDICA “EasyRA Chemistry Analyzer”

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

CLSI Guideline, EP5-A2 *Evaluation of Precision Performance of Clinical Chemistry Devices – Second Edition*

CLSI Guideline, EP9-A2 *Method Comparison and Bias Estimation Using Patient Samples – Second Edition*

L. Test Principle:

The Alkaline Phosphatase (ALP) enzyme hydrolyses 4-nitrophenyl phosphate substrate to form 4-nitrophenol and phosphates. The 4-nitrophenol component is

yellow in color at pH 10.4, with an absorbance peak at 405 nanometers. The rate of the formation of 4-nitrophenol is directly proportional to the Alkaline Phosphatase activity in the sample.

The Aspartate Aminotranferase (AST) enzyme catalyzes the transfer of the Aspartate amino group to α -Ketoglutarate (α -KG) with the formation of L-glutamate and oxaloacetate (OAA). The OAA is then reduced to L-malate by reacting with NADH in a reaction catalyzed by malate dehydrogenase (MDH). The amount of NADH that is oxidized to NAD reduces the sample absorbance at 340 nanometers. This decrease is directly proportional to the activity of AST in the sample.

The α -Amylase (AMY) enzyme hydrolyses the chromogenic substrate, 2-chloro-4-nitrophenol- α -D-maltotrioxide to form 2-Chloro-4-nitrophenol, which can be detected spectrophotometrically at 405 nanometers to give a direct measurement of α -amylase activity in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Serum and plasma- Precision studies were performed on the EasyRA analyzer in conjunction with the matrix comparison study with lithium heparin tubes. Duplicate plasma and serum samples from the method studies were calculated for average SD for 3 partitioned bins covering the ranges tested. The average SD in each of the 3 bins for both plasma and serum are comparable.

Alkaline Phosphatase			
	Low	Medium	High
Sample Range (U/L)	8-60	60-75	75-800
No. of Samples	22	25	27
No. of Replicates	2	2	2
Serum Mean	44.6	67.2	248.3
Serum SD	2.92	3.16	3.55
Serum % CV	6.5	4.7	1.4
Plasma Mean	39.8	61.8	246.5
Plasma SD	3.52	4.04	5.02
Plasma % CV	8.8	6.5	2.0

Aspartate Aminotranferase			
	Low	Medium	High
Sample Range (U/L)	5.5-17.5	17.5-25	25-400
No. of Samples	23	27	21

No. of Replicates	2	2	2
Serum Mean	14.4	20.5	91.9
Serum SD	1.60	1.20	1.20
Serum % CV	11.1	5.9	1.3
Plasma Mean	14.5	20.3	89.8
Plasma SD	1.18	1.23	0.96
Plasma % CV	8.1	6.0	1.1

Amylase			
	Low	Medium	High
Sample Range (U/L)	2-50	50-65	65-1200
No. of Samples	32	19	27
No. of Replicates	2	2	2
Serum Mean	38.1	56.7	342.4
Serum SD	0.47	0.69	4.74
Serum % CV	1.2	1.2	1.4
Plasma Mean	35.1	52.5	342.3
Plasma SD	0.63	0.65	3.66
Plasma % CV	1.8	1.2	1.1

In addition, a simplified within-run precision study was performed on the EasyRA analyzer by analyzing three plasma patient samples using lithium heparin tubes (N=20). The within-run precision data is summarized in the table below:

Analyte	Mean (U/L)	SD	CV
Alkaline Phosphatase	Level 1 - 176	Level 1 - 3.1	Level 1 - 1.78
	Level 2 - 267	Level 2 - 4.9	Level 2 - 1.83
	Level 3 - 600	Level 3 - 3.7	Level 3 - 0.62
Aspartate Aminotransferase	Level 1 - 74.8	Level 1 - 1.43	Level 1 - 1.92
	Level 2 - 140	Level 2 - 1.28	Level 2 - 0.91
	Level 3 - 338	Level 3 - 2.61	Level 3 - 0.77
Amylase	Level 1 - 132	Level 1 - 0.60	Level 1 - 0.45
	Level 2 - 393	Level 2 - 2.0	Level 2 - 0.51
	Level 3 - 835	Level 3 - 13.4	Level 3 - 1.60

b. Linearity/assay reportable range:

Plasma - Linearity studies were not conducted in plasma. See previously cleared linearity data in k080874 (Alkaline Phosphatase and Aspartate Aminotransferase) and k080823 (Amylase) for serum samples. The linear reportable ranges for each assay are summarized below.

Linear Reportable Range		
Alkaline Phosphatase	Aspartate Aminotransferase	Amylase
8 to 800 U/L	5.5 to 400 U/L	2 to 1200 U/L

An extended linearity study was performed for all analytes with the EasyRA analyzer to evaluate accuracy and precision. The sponsor recommends a dilution of 1:2 when the patient Alkaline Phosphatase, Aspartate Aminotransferase and Amylase results in plasma fall outside the upper measuring range of 800 U/L, 400 U/L and 1200 U/L, respectively. A dilution study was performed for Alkaline Phosphatase on five different spiked patient plasma samples to increase the Alkaline Phosphatase level in the range of 880 to 1385 U/L, for Aspartate Aminotransferase five different spiked patient plasma samples to increase the Aspartate Aminotransferase level in the range of 455 to 767 U/L and for Amylase five different spiked patient plasma samples to increase the Amylase level in the range of 1,500 to 2,000 U/L.

Each sample was then diluted with saline at 1:2 dilution by the analyzer or manually. Each diluted sample was run in triplicate on two EasyRA analyzers. The % recovery range of the system for each analyte is provided in the table below:

EasyRA Percentage Recovery		
Alkaline Phosphatase	Aspartate Aminotransferase	Amylase
99.7 to 101.5	97.7 to 98.8	99.2 to 101.7

In addition, a simplified within-run precision study was performed in the extended linearity range for all analytes by analyzing three plasma samples, twenty consecutive times. The within-run precision data is summarized in the table below:

Analyte	Mean	SD	CV
Alkaline Phosphatase	Level 1 - 1031	Level 1 - 12.5	Level 1 - 1.22
	Level 2 - 1174	Level 2 - 11.0	Level 2 - 0.94
	Level 3 - 1413	Level 3 - 16.5	Level 3 - 1.17
Aspartate Aminotransferase	Level 1 - 474	Level 1 - 3.70	Level 1 - 0.78
	Level 2 - 593	Level 2 - 7.57	Level 2 - 1.28
	Level 3 - 729	Level 3 - 7.36	Level 3 - 1.01
Amylase	Level 1 - 1410	Level 1 - 14.0	Level 1 - 0.99
	Level 2 - 2007	Level 2 - 17.5	Level 2 - 0.87
	Level 3 - 2180	Level 3 - 21.4	Level 3 - 0.98

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Calibrators were previously cleared under k080874 (Alkaline Phosphatase and Aspartate Aminotransferase) and k080823 (Amylase).
 - d. *Detection limit:*
Limit of detection studies were not conducted for plasma. See cleared serum data under k080874 (Alkaline Phosphatase and Aspartate Aminotransferase) and k080823 (Amylase).
 - e. *Analytical specificity:*
Plasma interference studies were not performed. See previously cleared interference data in k080874 (Alkaline Phosphatase and Aspartate Aminotransferase) and k080823 (Amylase) for serum samples.
 - f. *Assay cut-off:*
Not applicable
2. Comparison studies:

- a. *Method comparison with predicate device:*

Plasma – See previously cleared method comparison data in k080874 (Alkaline Phosphatase and Aspartate Aminotransferase) and k080823 (Amylase) for serum samples. Plasma matrix comparison data is provided below in part (b) of this section.

- b. *Matrix comparison:*

Plasma (Lithium Heparin)- A matrix comparison study was performed in conjunction with CLSI EP9-A2 guidelines using lithium heparin tubes. The study was conducted with human plasma and serum samples. Seventy-four total samples (58 unaltered and 16 altered samples) were analyzed for Alkaline Phosphatase; seventy-one total samples (59 unaltered and 12 altered samples) were analyzed for Aspartate Aminotransferase and seventy-eight total samples (62 unaltered and 16 altered samples) were analyzed for Amylase. Each sample was analyzed in duplicate using the EasyRA chemistry analyzer. One single set of plasma samples were used as test samples, while duplicate serum samples were used as references. Results of the linear regression correlations are as follows:

Analyte	Slope	Y-intercept	R ²	Sample Range (U/L)
ALP	1.0284	-6.3606	0.9902	13 to 764
AST	0.9741	+0.4669	0.9975	9.9 to 351.5
AMY	1.0247	-5.177	0.9985	4 to 1061

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:

The following reference is listed in the package insert: Tietz NW. *Textbook of Clinical Chemistry*, 2nd ed. WB Saunders and Co., Philadelphia, PA, p. 831-832 (1994).

Reference ranges for analytes in this review are as follows:

Analyte	Normal Range in serum
Alkaline Phosphatase	34 to 114 U/L (Adults)
Aspartate Aminotransferase	8 to 40 U/L
Amylase	25 to 94 U/L

N. Proposed Labeling:

The labeling is sufficient and 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.