

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

A. 510(k) Number:

k123802

B. Purpose for Submission:

Total Bilirubin: Addition of plasma to the already cleared device (k080810)
Direct Bilirubin: Addition of plasma to the already cleared device (k080810)
Creatine Kinase: Addition of plasma to the already cleared device (k080874)

C. Measurand:

Total Bilirubin (TBIL), Direct Bilirubin (DBIL), Creatine Kinase (CK)

D. Type of Test:

Quantitative colorimetric chemistry tests

E. Applicant:

Medica Corporation

F. Proprietary and Established Names:

EasyRA Total Bilirubin Reagent
EasyRA Direct Bilirubin Reagent
EasyRA Creatine Kinase Reagent

G. Regulatory Information:

Device Classification Name	Regulation section	Classification	Product Code	Panel
Total Bilirubin	21 CFR § 862.1110	II	CIG	Chemistry (75)
Direct Bilirubin	21 CFR § 862.1110	II	CIG	Chemistry (75)
Creatine Kinase	21 CFR § 862.1215	II	CGS	Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

EasyRA Total Bilirubin Reagent

The EasyRA TBIL reagent is intended for the quantitative determination of Total Bilirubin in human serum and plasma of adults on the MEDICA “EasyRA Chemistry Analyzer” in clinical laboratories. Bilirubin measurements are used in the diagnosis and treatment of liver, hemolytic, hematological, and metabolic disorders, including hepatitis and gall bladder block. For *in vitro* diagnostic use only.

EasyRA Direct Bilirubin

The EasyRA DBIL reagent is intended for the quantitative determination of Direct Bilirubin (DBIL) in human serum and plasma of adults on the MEDICA “EasyRA Chemistry Analyzer” in clinical laboratories. Bilirubin measurements are used in the diagnosis and treatment of liver, hemolytic, hematological and metabolic disorders, including hepatitis and gall bladder block. For *in vitro* diagnostic use only.

EasyRA Creatine Kinase

The EasyRA CK reagent is a device intended for the quantitative determination of Creatine Kinase (CK) in human serum and plasma, using the MEDICA “EasyRA Chemistry analyzer” in clinical laboratories. Measurements of CK are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy. For *in vitro* diagnostic use only.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

Medica EasyRA Analyzer

I. Device Description:

The EasyRA TBIL reagent kit is packaged as two ready to use reagents, R1 and R2. The formulation of each reagent is presented in the following table:

	Reactive Ingredients	Concentration
R1	NaCl	154 mmol/L
	HCl	190 mmol/L
	Surfactants and Preservatives	
R2	HCl	417 mmol/L
	2,4- dichlorophenyldiazonium salt	5 mmol/L
	Surfactant	

The EasyRA DBIL reagent kit is packaged as two ready to use reagents, R1 and R2. The formulation of each reagent is presented in the following table:

	Reactive Ingredients	Concentration
R1	EDTA-Na ₂	0.1 mmol/L
	NaCl	154 mmol/L
	Sulfamic acid	100 mmol/L
R2	2,4 – dichlorophenyldiazonium salt	5 mmol/L
	HCl	0.9 mmol/L
	EDTA – Na ₂	0.13 mmol/L

The EasyRA CK reagent kit is packaged as two ready to use reagents, R1 and R2. The formulation of each reagent is presented in the following table:

	Reactive Ingredients	Concentration
R1	Imidazole Buffer (pH 6.7)	100 mmol/L
	D-Glucose	20 mmol/L
	N-Acetyl-L-Cysteine	20 mmol/L
	Magnesium Acetate	10.0 mmol/L
	NADP	2.0 mmol/L

	EDTA	2.0 mmol/L
	Hexokinase (Baker's yeast)	2500 U/L
R2	Imidazole Buffer (pH 6.7)	100 mmol/L
	Creatine phosphate	30 mmol/L
	ADP	2.0 mmol/L
	AMP	5.0 mmol/L
	Diadenosine pentaphosphate	10.0 mmol/L
	Glucose-6-PDH (Baker's yeast)	1500 U/L
	EDTA	2.0 mmol/L

J. Substantial Equivalence Information:

New Device	Predicate Device Name	Predicate K Number(s)
EasyRA Total Bilirubin Reagent	EasyRA Total Bilirubin Reagent	k080810
EasyRA Direct Bilirubin	EasyRA Direct Bilirubin Reagent	k080810
EasyRA Creatine Kinase Reagent	EasyRA Creatine Kinase Reagent	k080874

Comparison with predicate:

Characteristic	Predicate device: EasyRA Total Bilirubin Reagent (k080810)	Candidate device: EasyRA Total Bilirubin Reagent
Intended Use	Intended for the quantitative determination of Total Bilirubin in human serum, using the MEDICA "EasyRA Chemistry Analyzer" in clinical laboratories	Same
Sample Type	Serum	Serum, Plasma
Reagent	Liquid Ready to use	Same
Assay Principle	Non-enzymatic reaction based on the binding of the analyte to an organic/inorganic compound to produce a chromogen at endpoint.	Same

	The chromogen absorbs light of specific wavelength and the resulting absorbance is measured.	
Analytical Range	0.08 – 20 mg/dL	Same

Characteristic	Predicate device: EasyRA Direct Bilirubin Reagent (k080810)	Candidate device: Easy RA Direct Bilirubin Reagent
Intended Use	Intended for the quantitative determination of Direct Bilirubin in human serum, using the MEDICA “EasyRA Chemistry Analyzer” in clinical laboratories	Same
Sample Type	Serum	Serum, Plasma
Reagent	Liquid ready to use	Same
Assay Principle	Endpoint	Same
Analytical Range	0.06 – 10 mg/dL	Same

Characteristic	Predicate device: EasyRA Creatine Kinase Reagent (k080874)	Candidate device: EasyRA Creatine Kinase Reagent
Intended Use	Intended for the quantitative determination of Creatine kinase in human serum, using the MEDICA “EasyRA Chemistry Analyzer” in clinical laboratories	Same
Sample Type	Serum	Serum, Plasma
Reagent	Liquid ready to use	Same
Assay Principle	Enzymatic reaction	Same
Linearity	3-1200 U/L	Same

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

Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline- Second Edition (CLSI EP5-A2)

L. Test Principle

EasyRA Total Bilirubin

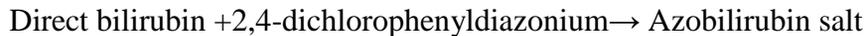
This endpoint reaction method measures total bilirubin (conjugated and unconjugated) binding to the 2,4-dichlorophenyldiazonium salt in the presence of surfactant to form azo-bilirubin.



The increase in absorbance at 550 nm is directly proportional to the Total Bilirubin concentration in the sample.

EasyRA Direct Bilirubin

This endpoint reaction is based on using a 2,4-dichlorophenyldiazonium salt as the diazo reagent:



Direct bilirubin (conjugated) binds with the diazo reagent to form azobilirubin. The increase in absorbance measured at 550 nm is proportional to the direct bilirubin concentration.

EasyRA Creatine Kinase

CK catalyzes transfer of phosphate groups from creatine phosphate to ADP to form ATP. The rate of production of ATP is measured by two coupled reactions. Hexokinase (HK) catalyzes the reaction of Glucose and ATP to form glucose-6-phosphate. The glucose-6-phosphate with NAD in the presence of glucose-6-phosphate dehydrogenase (G6PDH) forms 6-phosphogluconate and NADPH. The increase in NADPH absorbance at 340 nm is directly related to CK 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.

TBIL

	Low	Medium	High
Samples Range (mg/dL)	0.08 – 0.5 mg/dL	0.5 – 0.75 mg/dL	0.75 – 20 mg/dL
Number of Samples	23	23	16
Number of Replicates	2	2	2
Serum Mean	0.38	0.62	3.51
Serum SD	0.016	0.018	0.027
Serum % CV	4.2%	2.9%	0.77%
Plasma Mean	0.37	0.60	3.48
Plasma SD	0.017	0.013	0.030
Plasma %CV	4.6%	2.2%	0.86%

DBIL

	Low	Medium	High
Samples Range (mg/dL)	0.06 – 0.1 mg/dL	0.1 – 0.16 mg/dL	0.16 – 10 mg/dL
Number of Samples	20	15	17
Number of Replicates	2	2	2
Serum Mean	0.09	0.14	1.64
Serum SD	0.006	0.013	0.010
Serum % CV	6.7%	9.3%	0.61%
Plasma Mean	0.09	0.12	1.64
Plasma SD	0.007	0.008	0.010
Plasma %CV	7.8%	6.7%	0.61%

CK

	Low	Medium	High
Samples Range (U/L)	3 – 95 U/L	95 – 160 U/L	160 – 1200 U/L
Number of Samples	19	16	18
Number of Replicates	2	2	2
Serum Mean	68.0	121.5	370.4
Serum SD	0.63	1.06	1.69
Serum % CV	0.93%	0.87%	0.46%
Plasma Mean	64.3	118.5	369.2
Plasma SD	0.78	0.84	2.75
Plasma %CV	1.2%	0.71%	0.75%

In addition, a simplified within – run precision study was performed on the EasyRA analyzer by analyzing 3 plasma patient samples using lithium heparin tubes (N=20). The within – run precision data is summarized in the table below:

	Mean	SD	%CV
TBIL (mg/dL)	Level 1 – 0.78	Level 1 – 0.02	Level 1 – 2.16
	Level 2 – 4.82	Level 2 – 0.09	Level 2 – 1.82
	Level 3 – 12.49	Level 3 – 0.05	Level 3 – 0.43
DBIL (mg/dL)	Level 1 – 0.75	Level 1 – 0.01	Level 1 – 1.78
	Level 2 – 2.08	Level 2 – 0.03	Level 2 – 1.63
	Level 3 – 5.01	Level 3 – 0.02	Level 3 – 0.46
CK (U/L)	Level 1 – 10.66	Level 1 – 0.13	Level 1 – 1.26
	Level 2 – 75.45	Level 2 – 1.05	Level 2 – 1.39
	Level 3 – 942.90	Level 3 – 4.92	Level 3 – 0.52

b. *Linearity/assay reportable range:*

Plasma – Linearity studies were not conducted in plasma. See previously cleared linearity data in k080810 (TBIL and DBIL) and k080874 (CK) for serum samples. The linear reportable ranges for each assay are summarized below.

	TBIL	DBIL	CK
Linear Reportable Range	0.08 – 20 mg/dL	0.06 – 10 mg/dL	3 – 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 TBIL, DBIL, and CK results in plasma fall outside the upper measuring range of 20 mg/dL, 10 mg/dL and 1200 U/L, respectively. A dilution study was performed for TBIL on 5 different patient plasma samples spiked with standard TBIL stock solution to increase the TBIL level in the range of 20 to 40 mg/dL, for DBIL 5 different patient plasma samples were spiked with standard DBIL stock solution to increase the DBIL level in the range of 10 to 20 mg/dL, and for CK 5 different patient plasma samples were spiked with standard CK stock solution to increase the CK level in the range of 1200 to 2400 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 % Recovery
TBIL	98.77 to 101.01
DBIL	98.02 to 100.82
CK	101.00 to 102.79

In addition a simplified within-run precision study was performed in the extended linearity range for all analytes by analyzing 3 plasma samples, 20 consecutive times. The within-run precision data is summarized in the table below:

	Mean	SD	%CV
TBIL	Level 1 – 29.46	Level 1 – 0.21	Level 1 – 0.72
	Level 2 – 33.06	Level 2 – 0.34	Level 2 – 1.04
	Level 3 – 39.45	Level 3 – 0.27	Level 3 – 0.68
DBIL	Level 1 – 13.23	Level 1 – 0.07	Level 1 – 0.55
	Level 2 – 16.16	Level 2 – 0.13	Level 2 – 0.79
	Level 3 – 18.83	Level 3 – 0.12	Level 3 – 0.66
CK	Level 1 – 1398.95	Level 1 – 9.92	Level 1 – 0.71
	Level 2 – 1706.65	Level 2 – 12.52	Level 2 – 0.73
	Level 3 – 2050.40	Level 3 – 11.78	Level 3 – 0.57

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

Calibrators were previously cleared under k080810 (TBIL and DBIL) and k080874 (CK)

d. *Detection limit:*

Limit of detection studies were not conducted for plasma. See previously cleared serum data under k080810 (TBIL and DBIL) and k080874 (CK)

e. *Analytical specificity:*

Plasma interference studies were not performed. See previously cleared interference data in k080810 (TBIL and DBIL) and k080874 (CK) 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 k080810 (TBIL and DBIL) and k080874 (CK) for serum samples. 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. 62 total samples (56 unaltered and 6 altered samples) were analyzed for TBIL, 52 total samples (47 unaltered and 5 altered samples) were analyzed for DBIL, and 51 total samples (46 unaltered and 5 altered samples) were analyzed for CK. 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	Intercept	R ²	Sample Range
TBIL	0.9952	-0.0079	0.9998	0.17 to 16.78 mg/dL
DBIL	1.0064	-0.01	0.9992	0.07 to 9.95 mg/dL
CK	1.0081	-4.0906	0.9986	10 to 931 U/L

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:

EasyRA Total Bilirubin: Adult: 0.2 – 1.0 mg/dl¹

EasyRA Direct Bilirubin: 0.0 – 0.20 mg/dL¹

EasyRA Creatine Kinase: Male: 24-195 U/L, Female: 24-170 U/L²

The expected serum values for all the analytes were cited from the following references:

¹Burtis, C.A. and Ashwood, E.R. (Eds), Tietz Textbook of Clinical Chemistry, 2nd edition, W.B. Saunders CO., Philadelphia (1994).

²Tietz NW. Editor, Clinical Guide to Laboratory Tests, 3rd ed., WB Saunders and Co., Philadelphia, PA, (1995) p. 180.

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.