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

A. 510(k) Number:

K111363

B. Purpose for Submission:

New Device

C. Measurand:

Propoxyphene

D. Type of Test:

Qualitative and Semi-quantitative propoxyphene enzyme immunoassay

E. Applicant:

Medica Corp.

F. Proprietary and Established Names:

EasyRA Propoxyphene Reagent, EasyRA Propoxyphene Calibrators, EasyRA Propoxyphene QC Material

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JXN	Class II	21 CFR 862.3700 Propoxyphene test system	91
DLJ	Class II	21 CFR 862.3200 Clinical toxicology calibrator	91
LAS	Class I (reserved)	21 CFR 862.3280 Clinical toxicology control material	91

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The EasyRA Propoxyphene (PPX) reagent is intended for the qualitative and semi-quantitative measurement of Propoxyphene in human urine, using MEDICA's EasyRA Chemistry Analyzer in clinical laboratories. The cut-off point is 300ng/ml, and the assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas Chromatography/mass spectrometry (GC/MS) or Liquid Chromatography/mass spectrometry (LC/MS) are the preferred confirmatory method.

The semi-quantitative mode is intended to enable laboratories to determine the appropriate dilution of the specimen for confirmation by a reference method such as GCMS or LC/MS and to allow laboratories to establish effective quality control procedures for the PPX assay.

Medica's Propoxyphene (PPX) Calibrators are intended for the calibration of the PPX Enzymatic Immunoassay to estimate propoxyphene in human urine, using Medica's PPX reagent on the EasyRA clinical chemistry analyzer.

Medica's Propoxyphene (PPX) QC Materials are intended for the validation of the PPX Enzymatic Immunoassay to estimate propoxyphene in human urine, using Medica's PPX reagent and PPX calibrator on the EasyRA clinical chemistry analyzer.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Medica EasyRA analyzer

I. Device Description:

The reagents are liquid ready to use. R1 contains a monoclonal anti-propoxyphene mouse antibody, glucose-6-phosphate (G6P), Nicotinamide adenine dinucleotide (NAD), stabilizers and preservatives. R2 contains Propoxyphene-labeled glucose-6-phosphate dehydrogenase (G6PDH), stabilizers and preservatives.

Controls and calibrators are human urine based, liquid ready to use, spiked with various concentrations of propoxyphene.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Lin-Zhi International, Inc. Simultaneous Barbiturate-Methadone-Benzodiazepine-Propoxyphene (BMBP) Multiple Analyte Enzyme Immunoassay

Lin-Zhi International, Inc. Propoxyphene Calibrators
Lin-Zhi International, Inc. Propoxyphene Controls

2. Predicate 510(k) number(s):

k033885, k023316

3. Comparison with predicate:

Reagent Similarities and Differences		
Item	Submitted device: Easy RA PPX Reagent	Predicate Device: Propoxyphene reagent
Intended Use and indications for use	The Propoxyphene Enzyme Immunoassay is intended for the qualitative and semi-quantitative measurement of Propoxyphene, a pain-relieving drug, in human urine, using the EasyRA clinical chemistry analyzer.	Same
Sample type	Urine	Urine
Wavelength	340 nm	340 nm
Reaction type	Enzymatic Immunoassay	Enzymatic Immunoassay
Reagent storage	2 – 8 ^{0}C	2 – 8 ^{0}C
Test Methodology	The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the drug concentration in the sample is measured in terms of enzyme activity.	The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the drug concentration in the sample is measured in terms of enzyme activity.
Reagent Similarities and Differences		

Item	Submitted device: Easy RA PPX Calibrator and Control	Predicate Device:
Intended Use	The propoxyphene Calibrators are intended for the calibration of the PPX Enzymatic Immunoassay to quantitate propoxyphene in human urine, using Medica's PPX reagent on the EasyRA chemistry analyzer. The Propoxyphene QC controls are intended for the validation of the PPX Enzymatic Immunoassay to determine Propoxyphene in human urine, using Medica's PPX reagent on the EasyRA chemistry analyzer.	Same
Matrix	Urine	Urine
Reagent storage	2 – 8 ^{0}C	2 – 8 ^{0}C

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

None were referenced.

L. Test Principle:

The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenate (G6PDH) for a fixed amount of mouse antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the drug concentration in the sample is measured in terms of enzyme activity.

In the absence of drug in the sample, propoxyphene-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when free drug is present in the sample, antibody will bind to free drug, and the unbound propoxyphene-labeled G6PDH then exhibits its maximal enzyme activity.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-run and total precision were performed by analyzing nine levels of urine samples spiked with propoxyphene to 75, 150, 225, 300, 375, 450, 525, and 600 ng/mL on a Medica EasyRA analyzer. Full calibration with five level calibrators was performed to generate calibration curves for the semi-quantitative samples. The same samples were tested qualitatively using a one level (300 ng/mL) calibrator. Each sample was tested twice each morning and twice each afternoon for 20 days. The results are summarized below.

Qualitative

Target conc. (ng/ml)	0	75	150	225	300	375	450	525	600
Pos/Neg	0/80	0/80	0/80	0/80	1/79	80/0	80/0	80/0	80/0

Semi-quantitative

Target conc. (ng/ml)	0	75	150	225	300	375	450	525	600
Pos/Neg	0/80	0/80	0/80	0/80	20/60	80/0	80/0	80/0	80/0
Within run %CV	N/A	5.10	2.44	1.38	1.65	1.45	1.69	1.65	2.60
Total %CV	N/A	5.80	2.86	2.22	2.16	2.13	2.16	2.37	3.45

b. Linearity/assay reportable range:

Recovery was evaluated by testing nine urine samples spiked with propoxyphene to concentrations ranging from 50 to 800 ng/mL. Each sample was tested n=10 and the average value was calculated and compared to the actual value of the spiked sample. The results are summarized below.

	Sample # 1	Sample # 2	Sample # 3	Sample # 4	Sample # 5	Sample # 6	Sample # 7	Sample # 8	Sample # 9
Target conc.	50ng/ml	100ng/ml	150ng/ml	200ng/ml	300ng/ml	400ng/ml	500ng/ml	600ng/ml	800ng/ml
Mean	56.3	98.0	143.8	210.1	324.6	429.7	522.8	633.0	868.2
SD	5.6	3.6	4.3	3.5	4.4	13.7	16.8	28.2	63.2
CV	10.0	3.7	3.0	1.7	1.3	3.2	3.2	4.5	7.3
% Recovery	112.6%	98.0%	95.9%	105.1%	108.2%	107.4%	104.6%	105.5%	108.5%

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

Calibrators and controls were previously cleared under k023316. Medica is re-labeling these products for use on the EasyRA analyzer and verifying the calibrator and control values of the previously cleared products on the EasyRA analyzer to ensure traceability of the calibrators and controls.

Accelerated and real time stability studies were performed and support Medica's labeled storage conditions and expiration dating.

d. Detection limit:

Performance at low drug concentrations in the semi-quantitative assay was

characterized by determination of recovery (see section b above).

e. Analytical specificity:

Medica performed two interference studies for the PPX assay. The first coved interference from ten endogenous substances. The second investigated the potential cross-reactivity of thirty drugs with the PPX reagent.

Interference from urine endogenous substances:

Ten endogenous substances, seven pH levels, and seven specific gravity levels were evaluated as potential interferants of the propoxyphene (PPX) semi-Quantitative Assay on the EasyRA analyzer. Medica evaluated the potential interference at urine propoxyphene levels of 150 ng/ml, 300 ng/ml, and 450 ng/ml. The pH and specific gravity interference was evaluated in urine samples containing 225 ng/ml, 300 ng/ml, and 375 ng/ml propoxyphene. The following substances did not demonstrate significant interferences at the concentrations shown.

Substance	Concentration Tested without significant interference
Ascorbic Acid	2.5 mg/dl
Creatinine	500 mg/dl
Glucose	1200 mg/dl
Hemoglobin	100 mg/dl
Albumin (HSA)	300 mg/dl
Oxalic Acid	0.5 mg/dl
Sodium Chloride	2300 mg/dl
Acetone	790 mg/dl
Ethanol	790 mg/dl

The pH interference testing showed not significant interference due to pH ranging from 4.5 to 8.0.

The specific gravity interference testing showed not significant interference due to specific gravities ranging from 1.005 to 1.031.

Interference from cross reactivity

Thirty substances were evaluated as potential interferants of the propoxyphene (PPX) assay on the EasyRA analyzer.

The following compounds had a cross reactivity of less than 0.01% when spiked into propoxyphene free urine and urine with propoxyphene levels of 225 and 375 ng/mL: Amitriptyline, Amphetamine, Bupropion, Ecgonine, Ephedrine, Codeine, Caffeine, Chlorpheniramine, Cocaine, Lidocaine,

Ranitidine, Meperidine, Valproic Acid, Methaqualonel, Nortriptyline, Phenobarbital, Imipramine, Promethazine, Acetaminophen, Chlorpromazine, Dextromethorphan, Acetylsalicylic acid, Benzoylecgonine, Methadone, Methamphetamine, Morphine, Oxazepam, PCP, Secobarbital.

Nor-propoxyphene cross reactivity is summarized below.

Substance	Nominal PPX value 0.0ng/ml		
	True PPX (ng/ml)	Read PPX (ng/ml)	% Cross Reactivity
Norproxyphene 620 ng/ml	0	279	45.06%

f. Assay cut-off:

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision section, 1.a, above.

2. Comparison studies:

a. Method comparison with predicate device:

For the method comparison study, human urine samples with LC/MS propoxyphene and norpropoxyphene values were obtained from a reference laboratory. The samples were tested using the EasyRA propoxyphene assay in both qualitative and semi-quantitative modes of operation and compared to the GC/MS results. The results are summarized below.

Semi-quantitative mode

	Low Neg by LC/MS (less than -50%)	Near Cutoff Negative by LC/MS (Between -50% and cutoff)	Near Cutoff Positive by LC/MS (Between cutoff and +50%)	High Positive by LC/MS (greater than +50%)	Percent Agreement with LC/MS
Pos	0	1	11	45	95%
Neg	54	7	0	0	100%

Qualitative results

	Low Neg by LC/MS (less than -50%)	Near Cutoff Negative by LC/MS (Between -50% and	Near Cutoff Positive by LC/MS (Between cutoff and	High Positive by LC/MS (greater than +50%)	Percent Agreement with LC/MS

		cutoff)	+50%)		
Pos	0	1	11	45	95%
Neg	54	7	0	0	100%

Discrepant Sample Results

Total LC/MS Value (ng/ml)	EasyRA Semi-Quantitative	EasyRA Qualitative
220	POS	POS

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:

Not applicable

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.