

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

A. 510(k) Number:

k111005

B. Purpose for Submission:

New assay

C. Measurand:

Ethanol (Ethyl Alcohol)

D. Type of Test:

Automated quantitative enzymatic assay

E. Applicant:

Medica Corporation

F. Proprietary and Established Names:

EasyRA Ethyl Alcohol Reagent

EasyRA Ethyl Alcohol Calibrator

EasyRA Ethyl Alcohol QC Material.

G. Regulatory Information:

1. Regulation section:

21 CFR 862.3040, Alcohol Test System;

21 CFR 862.3200, Clinical Toxicology Calibrator;

21 CFR 862.3280, Clinical Toxicology Control Material

2. Classification:

Class II, (Test System and Calibrator), Class I (control materials)

3. Product code:

DIC, DLJ, LAS

4. Panel:

Toxicology (91)

H. Intended Use:

1. Intended use(s):

See indications for use.

2. Indication(s) for use:

The EasyRA Ethanol Reagent is intended for the quantitative measurement of Alcohol (ETOH) in human urine using Medica's EasyRA Chemistry Analyzer in clinical laboratories. Alcohol measurements are used for the diagnosis and treatment of alcohol intoxication and poisoning.

The EasyCal Ethanol Calibrator is intended for the calibration of the Ethyl Alcohol Assay on the EasyRA Chemistry Analyzer for the quantitative determination of ethyl alcohol in urine

The EasyQC Ethanol Quality Control Material is intended for the validation of the Ethyl Alcohol assay, which is used on the EasyRA clinical chemistry analyzer for the quantitative determination of ethyl alcohol in urine.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

For use on the EasyRA Analyzer

I. Device Description:

Reagents supplied are liquid, ready-to-use and consist of the following:.

Buffer Reagent (R1):

Tris-based buffer (50 mM)

Sodium azide (0.09%) as preservative.

Enzyme Reagent (R2):

Alcohol dehydrogenase (ADH)

Nicotinamide adenine dinucleotide (NAD, 10 mM),

Sodium azide (0.09%) as preservative.

Stabilizers

The calibrator and control matrix is an aqueous solution. Positive calibrators and controls are spiked with pure ethanol.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Microgenics Corporation Ethanol Reagent, including calibrator and control materials

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

k923783

3. Comparison with predicate:

Feature	Easy RA Ethanol Reagent	Predicate Device k923783
Intended Use	Clinical chemistry reagent used to provide a quantitative measurement of Alcohol	Same
Clinical sample matrix	Urine	Serum, plasma, urine
Reagent type	Liquid ready-for-use	Same
Linearity range	10 – 500 mg/dL	Up to 600 mg/dL
Wavelength	340 nm	Same
Reaction type	Enzymatic	Same
Reagent storage	2 – 8 °C	Same
Test Methodology	An enzymatic reaction of ethanol with ADH in the presence of NAD ADH converts ethyl alcohol to acetaldehyde and reduces NAD to NADH. The rate of change in absorption of the NADH chromogen is monitored over time on the EasyRA, to establish the amount of alcohol present.	Same

Feature	EasyRA EtOH Calibrator	EtOH Calibrator
Intended Use	Intended for the calibration of Ethyl Alcohol Enzymatic Assay to quantitate ethyl alcohol.	Same
Sample	Urine	Serum, plasma, urine
Reagent type	Liquid ready-for-use	Same
Reagent storage	2 – 8 °C	Same
Test Methodology	The Ethyl Alcohol Calibrator is an aqueous based liquid, and ready to use. A reagent blank measurement functions as a negative calibrator establishing the EtOH zero level. The calibrator contains about 100mg/dL ethanol (lot specific) and is used to establish the reference value for the EtOH urine assay.	The Ethyl Alcohol Calibrators are aqueous based liquids, and ready to use. The calibrator and two controls are prepared by spiking known concentrations of ethanol into the negative calibrator matrix. The negative calibrator contains no EtOH. The second contains about 100mg/dL ethanol (lot specific) and is used to establish the reference value for the EtOH urine assay.

Feature	EasyRA EtOH Control Materials	EtOH Control Materials
Intended Use	The EasyQC Ethanol Quality Control Material is intended for the validation of the Ethyl Alcohol assay	same
Sample	Urine	Serum, plasma, urine
Reagent type	Liquid ready-for-use	Same
Reagent storage	2 – 8 °C	2 – 8 °C

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

CLSI Guidelines:

EP09-A2-Method Comparison and Bias Estimation Using Patient Samples

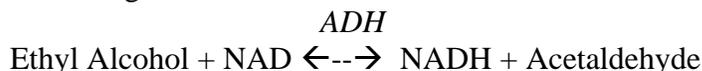
EP07-A2 Interference Testing in Clinical Chemistry

EP05-A2 Evaluation of Precision Performance of Quantitative Measurement Methods

EP06-A Evaluation of the Linearity of Quantitative Measurement Procedures

L. Test Principle:

Medica’s Ethyl Alcohol Enzymatic Assay is a two component ready-to-use liquid reagent based on alcohol dehydrogenase (ADH) unique enzymatic reaction. In the presence of nicotinamide adenine dinucleotide (NAD), ADH converts ethyl alcohol to acetaldehyde and reduces NAD to NADH. The ethyl alcohol concentration is directly proportion to the ADH activity. The rate of NADH formation is measured at 340 nm wavelength.



M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-Run, Run-to-Run, and Total precision were determined following CLSI EP5-A2 by analyzing four levels of urine samples spiked with pure (HPLC grade) ethanol. The study included an EasyRA analyzer and Medica’s EasyRA EtOH reagent and calibrator. For each of the four levels tested, two runs were conducted in the morning and two in the afternoon for 20 consecutive working days. Three calibrations were performed (on one analyzer) during the evaluation.

Within-run, day to day, and run to run analyses precision were evaluated, where:

Swr = Estimate of repeatability standard deviation (within-run precision)

Sdd = Estimate of between-day standard deviation

Srr = Estimate of between-run standard deviation

St =Estimate of within-device precision standard deviation

Results are shown in the tables below:

Grand mean	51.2 mg/dL
Swr	1.22
CVwr	2.40%
Sdd	1.36
CVdd	2.70%
Srr	0.00
CVrr	0.00%
St	1.83
CVt	3.57%

Grand mean	100.69 mg/dL
Swr	1.32
CVwr	1.31%
Sdd	2.46
CVdd	2.44%
Srr	1.02
CVrr	1.01%
St	2.97
CVt	2.95%

Grand mean	197.63 mg/dL
Swr	2.32
CVwr	1.17%
Sdd	4.27
CVdd	2.16%
Srr	1.28
CVrr	0.65%
St	5.02
CVt	2.54%

Grand mean	296.11 mg/dL
Swr	4.58
CVwr	1.55%
Sdd	4.47
CVdd	1.51%
Srr	4.74
CVrr	1.60%
St	7.96
CVt	2.69%

b. Linearity/assay reportable range:

Pure ethanol (HPLC grade) stock solution was used to spike a drug free urine pool to ethanol values of 500mg/dL (High) and 10mg/dL (Low). These solutions were subsequently mixed in pre-defined ratios using accurate volumetric techniques to make seven more solutions of known ethanol concentrations. The nine solutions tested covered the entire claimed linearity range.

Linearity was determined using the guidelines in CLSI EP6-A. Acceptance criteria are defined by the sponsor as +/-10% relative to the expected concentration (volumetrically determined) or within +/- 3 mg/dL – whichever is greater. Results are shown below.

Results:

Sample #	Assigned value mg/dL	Found value (mg/dL)	Percent recovery (found/assigned)	% Difference (Specification ±10% or ±3.0 mg/dL whichever is greater)
1	10.0	10.8	108%	-25.0% (0.8 mg/dL)
1		10.4	104%	-25.0% (0.4 mg/dL)
2	71.25	74.4	104%	-0.9%
2		71.9	101%	-0.9%
3	132.5	138.3	104%	0.6%
3		138.5	105%	0.6%
4	193.75	200.8	104%	0.8%
4		199.3	103%	0.8%
5	255.0	259.8	102%	0.7%
5		260.9	102%	0.7%
6	316.25	320.8	101%	0.5%
6		319.2	101%	0.5%
7	377.5	379.8	101%	0.2%
7		377.5	100%	0.2%
8	438.75	444.1	101%	-0.2%
8		444.7	101%	-0.2%
9	500.0	503.1	101%	-0.5%
9		496.5	99%	-0.5%

The claimed assay range is 10-500 mg/dL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):
 Calibrator and control materials were previously cleared under k032461. Stability claims and calibrator value assignments are the same as in that submission.

Control materials are further value assigned for Medica's Easy RA Assay. The value assignments are based on +/-10% of the median value obtained from multiple runs and multiple analyzers.

d. Detection limit:

Ethanol solutions above and below the lower claimed assay limit of 10 mg/dL were prepared by spiking pure ethanol into ethanol-free samples. At the claimed assay lower limit of 10 mg/dL, the percent recovery was within 7%, and CV was within 10% based on evaluation of five solutions with ethanol concentrations below 10 mg/dL tested in duplicate for each of five days. The lower assay limit of 10 mg/dL was established in the linearity studies (see section M1b).

e. Analytical specificity:

Three interference studies were performed to evaluate potentially interfering substances including those with a similar chemical structure to ethanol; endogenous substances, and urine preservatives typically used in clinical laboratories.

The interference studies were performed with drug-free urine samples spiked with ethanol to 20 mg/dL and to 100mg/dL by weight; each interfering solution tested was made by adding the corresponding volume of interferent from a stock solution. Data were collected with two EasyRA chemistry analyzers. Analytes and the highest concentrations tested are listed below:

Acetaldehyde	2000mg/dL
Acetone	2000mg/dL
n-Butanol	2000mg/dL
Ethylene glycol	2000mg/dL
Isopropanol	2000mg/dL
Methanol	2000mg/dL
n-Propanol	2000mg/dL
Ascorbic Acid	1000 mg/dL
Conjugated Bilirubin	10 mg/dL
Total Bilirubin	15 mg/dL
Creatinine	500 mg/dL
Glucose	1200 mg/dL
Hemoglobin	100 mg/dL
Human Albumin	300 mg/dL
Oxalic Acid	200 mg/dL
Sodium Chloride	2300 mg/dL
Gamma Globulin	500 mg/dL
Rivoflavin	7.5 mg/dL
pH	3.0 and 9.0 units

Changes in recovery of ethanol (i.e., interference) from these compounds were < 10%. Specific results are listed in the package insert. Cross-reactivities of > 10% were observed for acetaldehyde and n-propanol and this is listed in the package insert.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device

A study was performed to demonstrate the correlation between Medica's EtOH assay on the EasyRA chemistry analyzer and the EtOH predicate assay. A total of 68 patient urine specimens were tested using Medica's EtOH Reagent and calibrant on Medica's EasyRA analyzer and analyzed in duplicate on the Cobas-Mira using the Microgenics EtOH reagent and calibrant. Samples ranged from 13 to 460 mg/dL. The following are summary results of linear regression with 95% Confidence Intervals for slope and intercept:

Slope: 0.9914 [\pm .0097]; y- intercept: 0.3602 [\pm 1.55] mg/dL; coefficient of variation (r^2): 0.9982; Std. Error: 4.4750

b. Matrix comparison: This test is only for use with urine.

3. Clinical studies:

a. Clinical Sensitivity: Not applicable

b. Clinical specificity: See a, above.

c. Other clinical supportive data (when a. and b. are not applicable): Data regarding patient demographics and selection criteria were provided in the method comparison evaluation in the 510(k).

4. Clinical cut-off:

Not applicable

Expected values/Reference range:

The package insert states the following: Ethyl alcohol is not present in detectable concentrations in healthy adults who have not consumed ethanol.

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.