

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

A. 510(k) Number:

k070853

B. Purpose for Submission:

New Device

C. Measurand:

Ethyl Alcohol (Ethanol, ETOH)

D. Type of Test:

Enzymatic Alcohol Dehydrogenase for the quantitative measurement of ethyl alcohol

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Dimension Vista ETOH Flex reagent cartridge, Model K5022

G. Regulatory Information:

| Product Code | Classification | Regulation Section | Panel |
|--|----------------|---------------------------------------|-----------------------------|
| DIC- Alcohol Dehydrogenase, Specific Reagent For Ethanol Enzyme Method | Class II | 21 CFR 862.3040, Alcohol test system. | TX - 91 CLINICAL TOXICOLOGY |

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

The ETOH method is an *in-vitro* diagnostic test for the quantitative measurement of ethyl alcohol in human serum, plasma and urine.

Ethyl alcohol test results may be used in the diagnosis and treatment of alcohol intoxication and poisoning.

3. Special conditions for use statement(s):

For prescription use.

4. Special instrument requirements:

Dimension Vista® Integrated System

I. Device Description:

The Dimension Vista® ETOH Flex® reagent cartridge is a prepackaged *in-vitro* diagnostic test method that is specifically designed to be used on the Dade Behring Dimension Vista® System. The reagents contained in the Dimension Vista® ETOH Flex® reagent cartridge are: Reagent 1 which contains the buffering system and; Reagent 2 which contains alcohol dehydrogenase (ADH), the coenzyme nicotinamide adenine dinucleotide (NAD), buffer, preservatives, and stabilizers.

J. Substantial Equivalence Information:

| | Dimension Vista® ETOH Flex® reagent cartridge | Dimension® ALC Flex® reagent Cartridge (k904302) | Syva® Emit® II Plus Ethyl Alcohol Assay (k010960) |
|---------------------|---|---|---|
| Similarities | | | |
| Intended Use | The Dimension Vista® ETOH Flex® reagent cartridge is an <i>in-vitro</i> diagnostic test for the quantitative measurement of ethyl alcohol in human serum, plasma, and urine. Ethyl alcohol test results may be used in the diagnosis and treatment of alcohol intoxication and poisoning. | The ALC method used in the Dimension® clinical chemistry system is an <i>in vitro</i> diagnostic test intended to measure ethyl alcohol in human serum and supernatants from precipitated whole blood and to qualitatively detect ethyl alcohol in urine. | The EMIT® II Plus Ethyl Alcohol Assay is intended for use in the quantitative analysis of ethyl alcohol (ethanol) in human urine, serum, or plasma. |

| | | | |
|---------------------|--|--|---|
| | Dimension Vista® ETOH Flex® reagent cartridge | Dimension® ALC Flex® reagent Cartridge (k904302) | Syva® Emit® II Plus Ethyl Alcohol Assay (k010960) |
| Similarities | | | |
| Matrix | Plasma, serum, and urine. | Serum, supernatants from precipitated whole blood and urine. | Plasma, serum, and urine. |
| Sample | 4 uL | 3 uL | 4 uL |
| Principle | The ETOH method is based on an enzymatic reaction. | The ethyl alcohol (ALC) method is a modification of the alcohol dehydrogenase (ADH) enzymatic procedure. | The Emit®II Plus Ethyl Alcohol Assay is based on an enzymatic reaction. |
| Measurement | Bichromatic Rate | Bichromatic Rate | Bichromatic Rate |
| Differences | | | |
| Measuring Range | 3 - 300 mg/dL | 0 - 300 mg/dL | 10 - 600 mg/dL |

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

| STANDARDS |
|---|
| Title and Reference Number |
| BSI BS EN 13640 :Stability Testing of In Vitro Diagnostic Reagents |
| CLSI: Interference Testing in Clinical Chemistry; Approved Guideline (EP 7-A) |
| CLSI: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (EP09-A2) |
| CLSI: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline (EP5-A) |

| Other Standards | | | |
|---|---------------|-----------------|---|
| GUIDANCE | | | |
| Document Title | Office | Division | Web Page |
| Format for Traditional and Abbreviated 510(k)s - Guidance for Industry and FDA Staff | OIVD | | http://www.fda.gov/cdrh/ode/guidance/1567.html |
| In Vitro Diagnostic Devices: Guidance for the Preparation of 510(k) Submissions | OCER | | http://www.fda.gov/cdrh/manual/ivdmanul.html |

L. Test Principle:

The ETOH method is based on an enzymatic reaction. Reagent 1 contains the buffering system. Reagent 2 contains alcohol dehydrogenase (ADH), the coenzyme nicotinamide adenine dinucleotide (NAD), buffer, preservatives, and stabilizers. The ADH catalyzes the oxidation of ethyl alcohol to acetaldehyde. During this reaction, NAD is reduced to NADH. The absorbance due to NADH (proportional to the ETOH concentration) is determined using a two-filter (340-383 nm) bichromatic rate technique.

Ethyl alcohol + NAD <-----> acetaldehyde + NADH (absorbs at 340 nm)

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The sponsor conducted reproducibility studies according to CLSI Guideline for Evaluation of Precision Performance of Quantitative Measurement Methods (EP5-A2). Precision studies were conducted by testing two runs per day of three levels of a commercially available ethanol/ammonia control, serum pool, plasma pool and a urine pool (all in duplicate) for 20 days with one reagent lot. The mean values and standard deviations for repeatability and within-lab results are shown in the table below.

| | Low Control 42 mg/dL | | Med. Control 106 mg/dL | | High Control 270 mg/dL | | Serum Pool 107 mg/dL | | Plasma Pool 250 mg/dL | | Urine Pool 100 mg/dL | |
|-------------|-------------------------|------|---------------------------|------|---------------------------|------|-------------------------|------|--------------------------|-----|-------------------------|-----|
| | SD | CV% | SD | CV% | SD | CV% | SD | CV% | SD | CV% | SD | CV% |
| Mean | 41.68 | | 105.65 | | 269.89 | | 106.84 | | 273 | | 102 | |
| Within run | 1.02 | 2.46 | 2.14 | 2.02 | 4.05 | 1.50 | 2.12 | 1.98 | 8.0 | 2.9 | 2.0 | 2.0 |
| Between run | 0.77 | 1.84 | 1.01 | 0.95 | 1.95 | 0.72 | 1.99 | 1.86 | 1.3 | 0.5 | 1.6 | 1.5 |
| Between day | 0.52 | 1.25 | 1.33 | 1.26 | 3.41 | 1.27 | 1.20 | 1.13 | 2.7 | 1.0 | 0.0 | 0.0 |
| Within-lab | 1.38 | 3.32 | 2.71 | 2.57 | 5.64 | 2.09 | 3.14 | 2.94 | 8.5 | 3.1 | 2.5 | 2.5 |
| | | | | | | | | | | | | |

b. *Linearity/assay reportable range:*

Linearity was evaluated by comparing observed recovery (n=5) of spiked serum/plasma/urine samples serially diluted from 0 to 345 mg/dL. Urine, serum, and plasma specimens spiked with ethanol were used and prepared in ten percent increments. A linear regression analysis was then performed on

the data and plotted for visual confirmation of linearity. Linear regression comparing observed recovery versus theoretical recovery was used. The instrument generates a flag which states "Above Assay Range" or "Below Assay Range". In addition to this, automatic dilutions are performed by the instrument for results that fall outside the assay range. Automatic dilutions are defined in the method parameters and cannot be changed by an operator.

The data provided in the table below supports the claimed measuring range of 3 mg/dL to 300 mg/dL.

| Sample | Estimated spike ETOH mg/dL | Serum | | | Plasma | | | Urine | | |
|--------|----------------------------|-------------------|---------------------|---------------------|-------------------|---------------------|---------------------|-------------------|---------------------|---------------------|
| | | Theor. ETOH mg/dL | Observed ETOH mg/dL | % Recov. vs. Theor. | Theor. ETOH mg/dL | Observed ETOH mg/dL | % Recov. vs. Theor. | Theor. ETOH mg/dL | Observed ETOH mg/dL | % Recov. vs. Theor. |
| 1 | 0.0 | 0.0 | 1.4 | NA | 0.0 | -0.8 | NA | 0.0 | 0.9 | NA |
| 2 | 69.0 | 68.8 | 70.2 | 2.1 | 70.3 | 73.9 | 5.2 | 70.9 | 69.6 | -1.8 |
| 3 | 103.5 | 103.1 | 108.9 | 5.6 | 105.4 | 110.1 | 4.4 | 106.4 | 105.2 | -1.1 |
| 4 | 138.0 | 137.5 | 139.4 | 1.4 | 140.6 | 149.4 | 6.3 | 141.8 | 137.8 | -2.9 |
| 5 | 172.5 | 171.9 | 176.5 | 2.7 | 175.7 | 179.2 | 2.0 | 177.3 | 178.9 | 0.9 |
| 6 | 207.0 | 206.3 | 202.9 | -1.6 | 210.9 | 217.6 | 3.2 | 212.7 | 208.6 | -2.0 |
| 7 | 241.5 | 240.6 | 251.8 | 4.6 | 246.0 | 252.0 | 2.4 | 248.2 | 251.7 | 1.4 |
| 8 | 276.0 | 275.0 | 274.4 | -0.2 | 281.2 | 277.0 | -1.5 | 283.6 | 274.8 | -3.1 |
| 9 | 345.0 | 343.8 | 343.8 | 0.0 | 351.4 | 351.4 | 0.0 | 354.5 | 354.5 | 0.0 |

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

This device does not include calibrators. The sponsor recommends using calibrators by Dade Behring Inc. CHEM 3 Calibrator, Catalog Number KC130.

d. Detection limit:

The detection limit was defined as the concentration of two standard deviations of twenty replicates of a zero calibrator run on the Vista 104. The sponsors' results support the claimed detection limit of 3 mg/dL. The instrument will report samples that are less than 3 mg/dL as "less than 3 mg/dL".

e. Analytical specificity:

The sponsor conducted interference testing according to CLSI EP-7A2. Substances which potentially could interfere with the Dimension Vista® ETOH assay were spiked into aliquots of fresh serum and urine pools. Spiked samples were analyzed and the results were compared to control samples prepared without the potential interfering substance. Differences of less than 10% were considered non-interfering.

| Substance | Substance [conc.] | Ethyl Alcohol mg/dL | % Bias |
|--------------------------|-------------------|---------------------|--------|
| Hemoglobin (hemolysate) | 1000 mg/dL | 92 | <10% |
| Bilirubin (unconjugated) | 80 mg/dL | 96 | <10% |
| Bilirubin (conjugated) | 80 mg/dL | 95 | <10% |
| Lipemia (Intralipid) | 3000 mg/dL | 101 | <10% |

In addition to the above analytes, the sponsor determined that none of the following substances interfere with the ETOH method when present in serum and urine at the concentrations indicated. Differences (biases) due to these substances were less than 10% at ethanol concentrations of 100 mg/dL [21.7 mmol/L].

Serum:

Acetaminophen 20.0 mg/dL, Amikacin 8.0 mg/dL, Ampicillin 5.3 mg/dL, Ascorbic acid 6.0 mg/dL, Caffeine 6.0 mg/dL, Carbamazepine 3.0 mg/dL, Chloramphenicol 5.0 mg/dL, Chlordiazepoxide 1.0 mg/dL, Chlorpromazine 0.20 mg/dL, Cholesterol 503 mg/dL, Cimetidine 2.0 mg/dL, Creatinine 30 mg/dL, Dextran 40 6000 mg/dL, Diazepam 0.51 mg/dL, Digoxin 6.1 ng/mL, Erythromycin 6.0 mg/dL, Ethosuximide 25.0 mg/dL, Furosemide 6.0 mg/dL, Gentamicin 1.0 mg/dL, Heparin 3.0 U/mL, Ibuprofen 50 mg/dL, Immunoglobulin G (IgG) 5.0 g/dL, Lactate Dehydrogenase 237,500 U/L, Lactate 901 mg/dL, Lidocaine 1.2 mg/dL, Lithium 2.2 mg/dL, Mannitol 500 mg/dL, Nicotine 0.10 mg/dL, Penicillin G 25 U/mL, Pentobarbital 8.0 mg/dL, Phenobarbital 10.0 mg/dL, Phenytoin 5.0 mg/dL, Primidone 4.0 mg/dL, Propoxyphene 0.16 mg/dL, Protein (Albumin) 6.0 g/dL, Protein (Total) 12.0 g/dL, Salicylic Acid 60 mg/dL, Theophylline 4.0 mg/dL, Triglycerides 3000 mg/dL, Urea 500 mg/dL, Uric acid 20 mg/dL and Valproic Acid 50 mg/dL.

Urine:

Acetone 1.0 g/dL, Ascorbic acid 1.5 g/dL, Bilirubin 2.0 mg/dL, Creatinine 0.5 g/dL, Gamma globulin 0.5 g/dL, Glucose 2 g/dL, Hemoglobin 115 mg/dL, Human serum albumin 0.5 g/dL, Oxalic acid 0.1 g/dL, Riboflavin 7.5 mg/dL, Sodium chloride 6.0 g/dL, Urea 6.0 g/dL, Boric acid 1% w/v, Sodium azide 1% w/v and Sodium fluoride 1% w/v.

Potential cross-reactants were diluted to a desired concentration with water, and then spiked into ethanol spiked serum. The control sample was ethanol-spiked serum at desired concentrations. The following substances were evaluated for cross-reactivity with the ETOH method when present in serum containing 100 mg/dL of ethanol in the amounts shown. The percent cross-reactivity was calculated with the following equation:

$$\% \text{ Cross-reactivity} = \frac{\text{measured analyte (x units [SI])} - \text{control analyte (x units [SI])}}{\text{substance added}} \times 100$$

| Substance | Unit | % Cross Reactivity |
|------------------|------------|--------------------|
| Acetaldehyde | 2000 mg/dL | 0.1 |
| Acetone | 2000 mg/dL | 0.1 |
| n-Butanol | 500 mg/dL | 1.9 |
| Ethylene Glycol | 2000 mg/dL | 0.0 |
| Isopropanol | 2000 mg/dL | 0.4 |
| Methanol | 2000 mg/dL | 0.0 |
| n-Propanol | 47 mg/dL | 17.3* |
| Propylene Glycol | 2000 mg/dL | 0.0 |

*The device shows 17.3% cross reactivity with n-propanol.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Unaltered clinical patient serum and urine samples were used in the method comparison studies. The method comparison studies for 50 urine specimens were conducted at Dade Behring by R&D personnel. The method comparison studies for 117 serum specimens were conducted by trained laboratory personnel at an outside laboratory. All the samples were measured in singlet and only one specimen per patient was obtained. The correlation study between the device (ETOH) and the predicate yield for urine and serum yielded the following results.

| Matrix | n | Slope | Intercept | r | Device range (mg/dL) | Predicate range (mg/dL) |
|--------|-----|-------|-----------|-------|----------------------|-------------------------|
| Urine | 50 | 1.08 | -0.8 | 0.999 | 3.8- 298.0 | 5.2-276.0 |
| Serum | 117 | 1.06 | -0.9 | 0.999 | 9 – 299 | 9.1- 289 |

b. Matrix comparison:

A serum / plasma comparison test was performed for the Dimension Vista® ETOH Flex® assay. Twenty-seven samples ranging from 21.2 to 300 mg/dL were compared and yielded the following linear regression line. $Y = 0.96x + 2.60$ with a correlation constant of 0.993.

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 sponsor's expected value was established through literature. The pharmacological response to blood alcohol levels may vary from individual to individual. The fatal concentration has been reported to be greater than 400 mg/dL [86.8 mmol/L]. (Sunshine I., Methodology for Analytical Toxicology, CRC Press, Inc, Cleveland, OH, 1975 pp 152-153.)

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.