

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

A. 510(k) Number:

k073488

B. Purpose for Submission:

New Device

C. Measurand:

Apolipoprotein B assay

D. Type of Test:

Immunoassay

E. Applicant:

Diazyme Laboratories Division, General Atomics

F. Proprietary and Established Names:

Diazyme Apolipoprotein B Assay

A. Regulatory Information:

| Product Code | Classification | Regulation Section | Panel |
|--------------|------------------|--------------------|----------------|
| MSJ | Class II | 862.1475 | Chemistry (75) |
| JIT | Class II | 862.1150 | Chemistry (75) |
| JJX | Class I reserved | 862.1660 | Chemistry (75) |

H. Intended Use:

1. Intended use(s):

The Diazyme Apolipoprotein B Assay is intended for the quantitative determination of apolipoprotein B (apo B) in serum. It can be used as an aid for assessing the risk of coronary artery disease. For *in vitro* Diagnostic use.

Calibrator: For calibration of the Diazyme Apolipoprotein B Assay in serum.

Controls: To monitor the performance of Diazyme Apolipoprotein B Assay in serum.

2. Indication(s) for use:

See intended use (above).

3. Special conditions for use statement(s):

For Prescription Use Only.

4. Special instrument requirements:

Any instrument with a temperature control of 37 ± 0.5 °C that is capable of

reading absorbance accurately at 340 nm.

I. Device Description:

Included in the assay kit are two reagents, and a calibrator. Reagent 1 contains buffer including polyethylene glycol, Tris/HCl and Sodium chloride. Reagent 2 contains the anti-human-apoB antibody.

The calibrators are prepared from human serum. Each serum donor unit used in the preparation of this product has been tested and found to be non-reactive for HBsAg, HIV and HCV.

J. Substantial Equivalence Information:

1. Predicate device name(s):

K-Assay Apo B Assay

2. Predicate K number(s):

k993354

3. Comparison with predicate:

| Similarities | | |
|-------------------------|--|---------------------|
| Item or Characteristic | Device | Predicate (k993354) |
| Intended Use | Quantitative determination of Apo B to evaluate coronary disease risk | Same |
| Form | Lyophilized form | Same |
| Sample Type | Human Serum | Same |
| Calibrator Traceability | Diazyme Apolipoprotein B calibrator value is traceable to the WHO/IFCC Reference Standard. | Same |

| Differences | | |
|-----------------|---|---|
| Item | Device | Predicate |
| Test Principle | Turbidometric measurement of a immune complex of Apo B and specific antiserum at 340 nm | Turbidometric measurement of a immune complex of Apo B and specific antiserum at 600 nm |
| Measuring Range | 25 – 160 mg/dL | 25 – 250 mg/dL |

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

CLSI EP5-A: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline. Vol. 19 No.2, 2/1999

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline. Vol. 23 No. 16, 4/2003

CLSI EP7-A: Interference Testing in Clinical Chemistry; Approved Guideline. Vol. 22 No. 27, 12/2002

CLSI EP9-A: Method Comparison and Bias estimation Using Patient Samples; Approved Guideline. Vol. 15, No. 17, 12/1995

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline. Vol. 24 No. 34, 10/2004

L. Test Principle:

This method is based on the reaction of a sample containing human apo B and a specific antiserum to form an insoluble complex which can be measured turbidimetrically at 340 nm. The concentration of apo B can be determined by comparing sample results to a standard curve constructed from the absorbances of standards.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The precision of the Diazyme Apolipoprotein B assay was evaluated, according to CLSI EP5-A, in a study, using three levels of serum specimens containing low, medium and high levels of Apo B. They were tested with 2 runs per day in duplicates over 10 working days.

| | Level 1 | Level 2 | Level 3 |
|----------------------|----------------|-----------------|-----------------|
| Serum Testing | 24 mg/dL Apo B | 100 mg/dL Apo B | 155 mg/dL Apo B |
| Std. Deviation | 3.6 mg/dL | 15 mg/dL | 23.25 mg/dL |
| Within-Run Precision | CV% = 1.4% | CV% = 1.4% | CV% = 1.2% |
| Total Precision | CV% = 4.8% | CV% = 3.9% | CV% = 2.1% |

b. Linearity/assay reportable range:

The claimed measuring range of this device is 25- 160 mg/dL. Eleven levels of samples were prepared in triplicate by diluting a serum control containing 157 mg/dL Apo B with saline according to CLSI EP6-A guidelines. Linear Regression analysis results obtained were as follows: Slope = 0.988, Intercept = 1.203 with an $R^2 = 0.9992$.

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

Calibrator and Control Stability: The ApoB calibrator stability testing was performed in real time at 4°C, and as accelerated stability studies at 25°C and

37°C using two lots of the calibrator. Real-time stability tests are ongoing.

Calibrator Traceability: The Calibrator is traceable to WHO/IFCC standards.

d. Detection limit:

Limit of Detection studies were performed following CLSI EP17-A. Five (5) serum samples containing low ApoB were diluted 100X with 7.5% BSA in saline and tested with the ApoB reagent on the Hitachi 917 with 12 replicates each (a total of 60 measurements). The results are summarized as follows:

$$\text{LoD} = \text{LoB} + (1.645 * \text{SD Low Samples}) = 3.60 + (1.645 * 0.5556) = 3.60 + 0.91 = 4.51 \text{ mg/dL}$$

The LOD of the Diazyme ApoB assay was determined to be 4.51 mg/dL.

e. Analytical specificity:

Interference testing was performed per CLSI guideline EP7-A. The following compounds were tested up to the concentrations detailed below with normal serum (containing 70 mg/dL of ApoB). There was $\leq \pm 10\%$ deviation in the observed concentration of ApoB.

| Interference Substance | Concentration |
|------------------------|---------------|
| Ascorbic Acid | 10 mM |
| Bilirubin | 40 mg/dL |
| Bilirubin Conjugated | 40 mg/dL |
| Hemoglobin | 1000 mg/dL |
| Triglycerides | 1000 mg/dL |
| Apolipoprotein A-1 | 500 mg/dL |

Further, there was no cross-reactivity observed with Apo A-1 when tested up to a concentration of 500 mg/dL.

f. Assay cut-off:

Not Applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The individual patient serum samples used for this study were from a certified commercial source and the assay was performed on a Hitachi 917 analyzer.

To ensure the concentrations of Apo B were distributed across the reportable dynamic range claimed, additional Apo B samples were spiked with Apo B to achieve higher concentrations, or diluted with saline to reach lower concentrations. A total of 55 unaltered and 7 altered serum samples were used for the comparison experiment. The comparison results between the Diazyme Apolipoprotein B assay and the Kamiya Apo B reagent are summarized below:

For a total of 62 serum samples ranging from 29.6 to 241.1 mg/dL Apo B, the correlation coefficient between the two methods was 0.9864; the slope was 1.0143; and y intercept was -4.3806.

The study was also analyzed using Passing-Bablok regression and the results obtained were:

$$Y = -2.8942 + 1.0082 X$$

Intercept: -2.8942
95% CI : -7.6091 to 0.3990
Slope: 1.0082
95% CI : 0.9720 to 1.0512

- 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:
The sponsor claims a references range for Apolipoprotein B in adults of 63- 114 mg/dL.
Source citation: Fruchart, J-C (1986), Ann. Biol. Clin 44:116.

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.