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

A. 510(k) Number:
k082488

B. Purpose for Submission:
New 510(k)

C. Measurand:
Lipoprotein (a) [Lp(a)]

D. Type of Test:
Immunoturbidimetric

E. Applicant:
General Atomics

F. Proprietary and Established Names:
Diazyme Lp(a) Assay

G. Regulatory Information:
1. Regulation section:
   21CFR Sec.- 866.5600-Low-Density Lipoprotein Immunological Test System.
   21CFR Sec.-862.1150 Calibrator.
   21CFR Sec -862.1660 Quality control material (assayed and unassayed).

2. Classification:
   Class 2, 2 and 1 (reserved)

3. Product code:
   DFC - Lipoprotein, Low-Density, Antigen, Antiserum, Control
   JIT- calibrator, secondary
   JJX - single (specified) analyte controls (assayed and unassayed)

4. Panel:
   Chemistry (75)

H. Intended Use:
1. Intended use(s):
   See indication(s) for use below

2. Indication(s) for use:
   The Diazyme Lp(a) is intended as a latex enhanced Immunoturbidimetirc assay
   for the in vitro quantitative determination of lipoprotein(a) [Lp(a)] concentration

in human serum or plasma (EDTA) on Clinical Chemistry Systems. The measurement of Lp(a) is useful in evaluation lipid metabolism disorders and assessing atherosclerotic cardiovascular diseases in specific population, when used in conjunction with clinical evaluation.

Diazyme Lp(a) Control is intended for use in monitoring the quality control of results obtained with the Diazyme Lp(a) reagents by turbidimetry

Diazyme Lp(a) calibrator is intended for use in establishing the calibration curve for the Diazyme Lp(a) reagents by turbidimetry.

3. Special conditions for use statement(s):
   Prescription use

   Lp(a) values should be interpreted in conjunction with clinical evaluation and other lipoprotein tests when assessing atherosclerotic cardiovascular disease in specific populations.

   The effects of the impact of Apo A size heterogeneity on lipoprotein (a) measurements by this method have not been assessed.

4. Special instrument requirements:
   Performance data was provided for use with the Hitachi 717

I. Device Description:
Lipoprotein (a) Reagent Composition
    Reagent 1
    Glycine Buffer Solution

    Reagent 2
    Latex particles coated with anti-Lp(a) antibodies

Reagent Preparation
    1. The Lp(a) assay reagent provided is ready to use.
    2. Physiological saline is needed to dilute high Lp(a) samples.

Lipoprotein (a) Calibrator Set
    5 vials containing lyophilized calibrators with different Lp(a) concentrations ($\approx$ 6.5, 14.2, 31.4, 62.4, 83.8 mg/dL). 5 x 1.0 mL (after reconstitution)
    Each serum donor unit used in the preparation of this product has been tested using FDA approved methods and found to be non-reactive for HBsAg, HIV and HCV.

Lipoprotein (a) Control Set
    2 vials containing lyophilized calibrators with different Lp(a) concentrations (target range $\approx$ 17.3 - 23.5, 50.1 - 67.6 mg/dL) . 2 x 1.0 mL (after reconstitution)
    Each serum donor unit used in the preparation of this product has been tested using

FDA approved methods and found to be non-reactive for HBsAg, HIV and HCV.

J. Substantial Equivalence Information:
1. Predicate device name(s):
   Denka Lp(a) assay
   Dade Behring, N LP(a) Standard
   Kamiya Biomedical, K-Assay LP(a) Controls

2. Predicate 510(k) number(s):
   k013359
   k013126
   k023853

3. Comparison with predicate:
   Intended use

Diazyme Lp(a) Assay	Denka Lp(a) Assay	Equivalency
The Diazyme Lp(a) immunoassay is intended for the in vitro quantitative determination of Lipoprotein (a) in human serum and plasma.	The Lp(a) Assay is a latex in vitro diagnostic immunoassay for the quantitative determination of Lipoprotein (a) in human serum and plasma.	Same

Principle

Diazyme Lp(a) Assay	Denka Lp(a) Assay	Equivalency
The Diazyme Lipoprotein (a) Assay is based on a latex enhanced immunoturbidimetric assay. Lp(a) in the sample binds to specific anti-Lp(a) antibody, which is coated on latex particles, and causes agglutination. The degree of the turbidity caused by agglutination can be measured optically and is proportional to the amount of Lp(a) in the sample.	The Lp(a)-Latex Seiken Assay kit is a latex-enhanced immunoturbidimetric in vitro diagnostic assay. Lp(a) in the sample binds to the specific anti-Lp(a) antibody, which is adsorbed to latex particles and agglutinates. The agglutination is detected as an absorbance change when read on an automated chemistry analyzer (at 700 nm). The magnitude of the change is proportional to the quantity of Lp(a) in the sample. The actual concentration is then determined by interpolation from a calibration curve prepared from calibrators of know concentrations.	Same

Product Type

Diazyme Lp(a) Assay	Denka Lp(a) Assay	Equivalency
Calibrator, Reagent, Instrument	Calibrator, Reagent, Instrument	Same

Calibrator Comparison

Diazyme Lp(a) Assay	Denka Lp(a) Assay	Equivalency
Lyophilized form	Lyophilized form	Same

Control Comparison

Diazyme Lp(a) Assay	Denka Lp(a) Assay	Equivalency
Lyophilized form	Lyophilized form	Same

K. Standard/Guidance Document Referenced (if applicable):
CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices - EP05-A2
CLSI - Evaluation of the Linearity of Quantitative Analytical Methods - EP06-A
CLSI - Protocols for Determination of Limits of Detection and Limits of Quantitation - EP17-A

L. Test Principle:
The Diazyme Lipoprotein (a) Assay is based on a latex enhanced immunoturbidimetric assay. Lp(a) in the sample binds to specific anti-Lp(a) antibody, which is coated on latex particles, and causes agglutination. The degree of the turbidity caused by agglutination can be measured optically and is proportional to the amount of Lp(a) in the sample.

M. Performance Characteristics (if/when applicable):
1. Analytical performance:
   a. *Precision/Reproducibility:*
      The precision of the Diazyme Lp(a) Enzymatic Assay was evaluated according to Clinical and Laboratory Standards Institute EP5-A guideline. In the study, three levels of serum specimens containing about 17.2, 43.2, and 70.0 mg/dL Lp(a) respectively are tested with 2 runs per day with duplicates over 20 working days on Hitachi 717.

Within Run Precision (Sr)			
	Level 1: mg/dL Lp(a)	Level 2: mg/dL Lp(a)	Level 3: mg/dL Lp(a)
Number	80	80	80
Mean (mg/dL)	18.3	42.2	71.66
SD (mg/dL)	0.47	0.59	0.76
CV%	2.6	1.4	1.1

Within Run Precision (Sr)			
	Level 1: mg/dL Lp(a)	Level 2: mg/dL Lp(a)	Level 3: mg/dL Lp(a)
Number	80	80	80
Mean (mg/dL)	18.3	42.2	71.66
SD (mg/dL)	0.66	1.38	1.71
CV%	3.6	3.3	2.4

b. *Linearity/assay reportable range:*
Eleven levels of linearity set were prepared by diluting a serum control containing 100 mg/dL LP(a) with saline according to Clinical and Laboratory Standards Institute EP6-A to test a range from 5 to 100 mg/dL LP(a) and was shown to be linear. The following regression equation was obtained.

$$y = 0.9945x + 0.5997$$
$$R^2 = 0.9985$$

The assay has a linear range up to 100 mg/dL and a low reportable range to 5.44 mg/dL based on LOQ.

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

Calibrators
Using a single lot of predicate device reagents and calibrator, Diazyme Lp(a) master lot of calibrator materials were assigned values as follows. The calibrator materials were assayed as samples three times in triplicate on the Hitachi 717 Analyzer. For each calibrator level, mean values were calculated from the data points and assigned as the calibrator value. For each new lot of calibrator materials produced, the master lot or reference lot calibrator is used in conjunction with the reference lot of Diazyme reagents to test and verify calibrator value.

Controls
Using in-house reagents and calibrator, control materials were assigned values as follows. The control materials were assayed as samples three times in triplicate on the Hitachi 7171 analyzer with a single lot of released reagents and calibrator. Fer each control level, mean values were calculated from the data points and assigned as the target value.

Stability for both calibrators and controls is based on real time stability studies.

d. *Detection limit:*
The LOB, LOD, and LOQ of Diazyme LP(a) Assay was determined according to CLSI EP17-A: Protocols for Determination of Limits of

Detection and Limits of Quantitation; Approved Guideline on the Hitachi 717. LOB was determined using a BSA solution in phosphate buffered saline and tested twenty times each day for three days. The LOD was determined using low samples tested in replicates of four each day for three days. LOQ was determined using 6 samples ranging from 0.42 to 17.38 mg/dL and using a fitted curve to determine the value at 20% CV. The results obtained are as follows:

- The Limit of Blank (LOB) for Lp(a) assay is 0.64 mg/dL
- The Limit of detection (LOD) for Lp(a) assay is 1.14 mg/dL
- The Limit of Quantitation (LOQ) for Lp(a) assay is 5.44 mg/dL

  e. *Analytical specificity:*
  Two levels of Lp(a) 16 and 43 mg/dL were tested for interference from hemoglobin to 1000 mg/dL, Bilirubin to 40 mg/dL, conjugated Bilirubin to 40 mg/dL, triglyceride to 1000 mg/dL and Ascorbic Acid to10 mM with no interference based on ± 10% deviation from expected result.

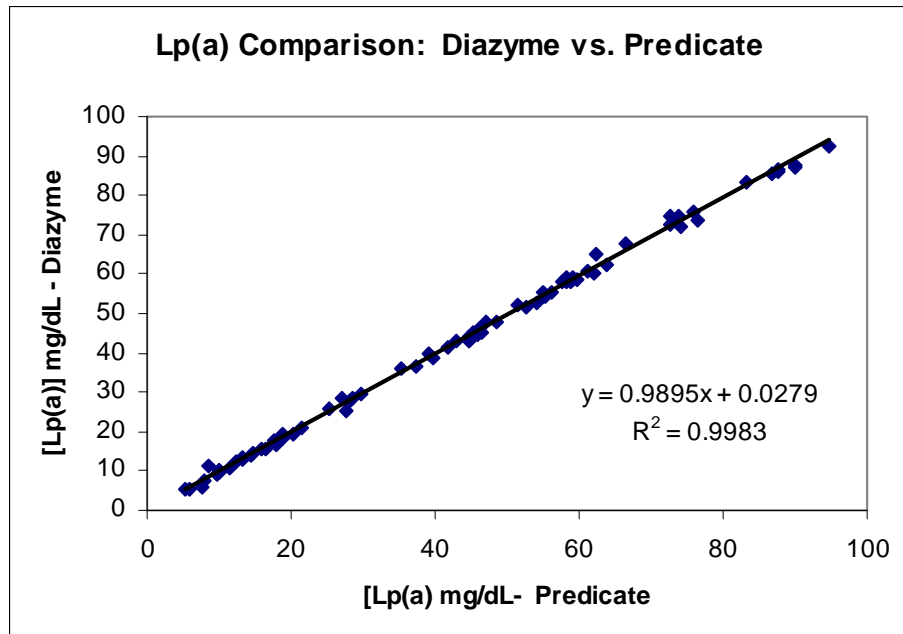 f. *Assay cut-off:*
  Not Applicable

2. Comparison studies:
  a. *Method comparison with predicate device:*

  To demonstrate method comparison, the Diazyme LP(a) Assay was tested with individual serum samples and with the Denka Lp(a)-Latex Seiken Assay and calibrator (k013359).

  A total of 76 serum samples were used for the comparison experiment. To ensure the concentrations of LP(a) distributed across the reportable dynamic range, some serum samples were spiked with stock solution of LP(a) or diluted with saline to targeted concentrations.

  LP(a) concentrations obtained with Diazyme LP(a) Enzymatic Assay are plotted against that obtained with Denka Seiken Lp(a) Reagent kit (Predicate) on HITACHI 717.

Lp(a) Comparison: Diazyme vs. Predicate

Chart: Y-axis labeled "[Lp(a)] mg/dL - Diazyme" (0 to 100), X-axis labeled "[Lp(a) mg/dL- Predicate" (0 to 100).

$y = 0.9895x + 0.0279$

$R^2 = 0.9983$

Conclusion: For the 76 serum samples with Lp(a) ranging from 5.21 mg/dL to 94.83 mg/dL, the correlation coefficient between the two methods was 0.9983, slope was 0.9895, and y intercept was 0.0279.

    b. Matrix comparison:
    Lp(a) levels of 20 sample pairs covering the assay range using EDTA plasma to serum yielded the following data analysis:
    $y = 1.044x + 0.0407 \ R^2 = 0.9803$

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:
    In the labeling the sponsor has cited published literature as follows: "Studies have shown the expected range for Lp(a) has been reported to be between 10 and 30 mg/dL. Some studies have indicated that Lp(a) concentrations in African Americans may differ from Caucasians with African American ranges higher."

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.