

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

A. 510(k) Number:

k072977

B. Purpose for Submission:

New device

C. Measurand:

Apolipoprotein A1 assay, calibrators, controls

D. Type of Test:

Quantitative

E. Applicant:

General Atomics

F. Proprietary and Established Names:

Diazyme Apolipoprotein A-I Assay

Diazyme Apolipoprotein A-I Calibrator

Diazyme Apolipoprotein A-I Controls

G. Regulatory Information:

1. Regulation section:

21 CFR § 862.1475 - Lipoprotein test system

21 CFR § 862.1150 - Calibrator

21 CFR § 862.1660 - Quality control material (assayed and unassayed)

2. Classification:

Class I, meets the limitations to the exemption 21 CFR 862.9(c)(4)

Class II

Class I, reserved

3. Product code:

MSJ - Apolipoproteins

JIT – Calibrator (secondary)

JJX - Single (specified) analyte controls (assayed and unassayed)

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The Diazyme Apolipoprotein A-I Assay is intended for the in vitro quantitative determination of apolipoprotein A-I (apo A-I) 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 A-I Assay in serum. For in vitro Diagnostic Use.

Controls: To monitor the performance of Diazyme Apolipoprotein A-I Assay in serum. For in vitro Diagnostic Use.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

Instrument with temperature control of 37°C capable of reading absorbance at 340 nm.

I. Device Description:

The assay consists two reagents, a buffer reagent and a reagent with anti-human-apo

A-I antibody. The calibrator consists of lyophilized human serum. The Apolipoprotein A-I Control Set is a three level, lyophilized, entirely human serum based control. Each serum donor unit used in the preparation of these products have been tested and found to be non-reactive for HBsAg, HIV and HCV. FDA approved methods have been used to conduct these test. Since no known test method can offer complete assurance that infectious agents are absent, this product should be treated as potentially infectious and handle in accordance with good laboratory practices using appropriate precautions. Preservatives have been added to inhibit microbial growth.

J. Substantial Equivalence Information:

1. Predicate device name(s):

K-Assay Apo AI Assay

K-Assay Apo A1/B calibrator set

Cliniqa Lipid Control

2. Predicate K number(s):

k993345, k993606, k061182

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	Quantitative determination apolipoprotein A1	Quantitative determination apolipoprotein A1
Calibrator	Lyophilized serum	Lyophilized serum
Sample type	Serum	Serum
Assay Methodology	immunoturbidimetric	immunoturbidimetric

Differences		
Item	Device	Predicate
Reportable range	20- 228 mg/dL	20 – 300 mg/dL
Measurement	Absorbance at 340 nm	Absorbance at 800 nm

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

Not applicable

L. Test Principle:

This method is based on the reaction of a sample containing human Apo A-I and

specific antiserum to form an insoluble complex which can be measured turbidimetrically at 340 nm. By constructing a standard curve from the absorbance of standards the concentration of Apo A-I can be determined.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The precision of the Diazyme Apolipoprotein A-I assay was evaluated according to Clinical and Laboratory Standards Institute (CLSI) EP5-A guideline. In the study, three levels of serum specimens containing approximately 80, 157, and 213 mg/dL Apo A-I respectively were tested with 2 runs per day in duplicates over 10 working days. The results are shown below

Within Run Precision

	Level 1:	Level 2:	Level 3:
n	40	40	40
Mean	80.18	157.29	212.98
SD	0.47	1.43	1.39
CV%	0.6%	0.9%	0.7%

Within-Laboratory Precision

	Level 1:	Level 2:	Level 3:
n	40	40	40
Mean	80.18	157.29	212.98
SD	2.65	2.81	4.73
CV%	3.3%	1.8%	2.2%

b. *Linearity/assay reportable range:*

Eleven levels of linearity samples were prepared by diluting a serum control containing 228 mg/dL Apo A-I with saline according to CLSI EP6-A guidelines. The linearity set was tested with the Diazyme Apo A-I Assay in triplicates. The results are shown below.

Dilution	Observed	Expected
Level 10	228.77	228.77
Level 9	210.13	205.893
Level 8	187.57	183.016
Level 7	160.43	160.139
Level 6	140.30	137.262

Level 5	116.23	114.385
Level 4	93.13	91.508
Level 3	68.83	68.631
Level 2	43.53	45.754
Level 1	19.93	22.877
Level 0	0.50	0

Linear regression was performed with the following results: $y = 1.019x - 1.176$, $R^2 = 0.999$. The claimed reportable range is from 20 – 228 mg/dL.

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

The Diazyme Apolipoprotein A-1 calibrator is traceable to the WHO/IFCC International Reference Materials for Apo A-1, SP-101. Value assignment was performed using reference calibrators provided by Northwest Lipid Metabolism & Diabetes Research Labs (NLMDRL). The values were also verified by NLMDRL.

The sponsor did not provide any traceability information for the values assigned to the controls. Control values were assigned by performing multiple runs, each with multiple replicates with a single lot of reagents and calibrators. Mean values and acceptable ranges were calculated for each control from this data.

Stability testing was performed and demonstrated that the calibrators, controls, and reagents are stable until the expiration date on the label when stored as instructed. The reagents have a shelf life of one year and are stable on board the Hitachi 917 for 60 days. Calibrators and controls have a shelf life of one year. Once reconstituted the calibrators and controls are stable for 7 days when stored at 2 – 8°C.

d. Detection limit:

To demonstrate the limit of the blank (LOB) of the Diazyme Apo A-I immunoturbidimetric assay, Apo A-I zero calibrator was tested in 12 replicates on Hitachi 917 and LOB was defined as the mean+3SD. The LOB was calculated as 1.44 mg/dL. To determine the limit of detection (LOD) serum samples containing low concentrations of ApoA-1 were tested with ApoA-1 reagent on Hitachi 917 with 12 replicates each. The LOD was defined as $LOD = LOB + (1.645 * SD \text{ Low Samples})$. The LOD was calculated as 1.58 mg/dL. The sponsor claims 20 mg/dL as the low end of the reportable range.

e. Analytical specificity:

To determine the level of interference from the substances normally present in human serum, Diazyme Apo A-I immunoturbidimetric assay was tested with

normal Apo A-I serum samples spiked with various concentrations of substances following CLSI EP7-A "Interference Testing in Clinical Chemistry". No interference was defined as a deviation of less than 10% from the interferant free sample. The following substances normally present in the serum showed no interference when tested at levels equal to the concentrations listed below.

Interfering Substance	Concentration
Ascorbic Acid	10 mM
Bilirubin	40 mg/dL
Bilirubin, conjugated	40 mg/dL
Hemoglobin	1000 mg/dL
Triglycerides	1000 mg/dL
Apolipoprotein A11	500 mg/dL

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed by testing individual serum samples with the Diazyme Apolipoprotein A-I Assay and the predicate device. To ensure the concentrations of Apo A-I were distributed across the reportable dynamic range claimed, additional Apo A-I samples were spiked with Apo A-I to achieve higher concentrations, or diluted with saline to reach lower concentrations. A total of 56 un-altered and 9 altered serum samples with concentrations that span the full reportable range were used for the comparison experiment. Linear regression was performed with the following results: $y = 0.908x + 2.813$, $R^2 = 0.979$. Due to the approximately 9% bias in the slope compared to the predicate device, each lab should establish its own reference range.

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 normal range of Apo A I is 120 – 176 mg/dL.

The package insert also instructs each lab to establish their own reference ranges as the normal range is dependent on geographical location.

(Provisional normal values recalculated on the basis of the CDC values C. 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.