

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

A. 510(k) Number: k043264

B. Purpose for Submission: Notification of intent to manufacture and market the device: LDL-EX SEIKEN Assay Kit

C. Measurand: Low Density Lipoprotein

D. Type of Test: Colorimetric

E. Applicant: Denka Seiken Co., LTD.

F. Proprietary and Established Names: Proprietary – LDL-EX Seiken Assay Kit. Established – Homogenous assay for low-density lipoprotein cholesterol test

G. Regulatory Information:

1. Regulation section: 21 CFR 862.1475 lipoprotein test system 21 CFR 862.1150 Calibrator
2. Classification: Class I – This device meets the limitations of exemptions from section 510(k) of the Food, Drug and Cosmetic Act (for assessing the risk of cardiovascular diseases) 21 CFR 826.9 (c) (4)
3. Product code: MRR
4. Panel: 75 - Chemistry

H. Intended Use:

1. Intended use(s): See indications for use below.
2. Indication(s) for use: The LDL-EX SEIKEN Assay kit is an in vitro diagnostic test for the quantitative determination of low density lipoprotein cholesterol (LDL-C) in human serum and heparinized or EDTA plasma. Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus, atherosclerosis, and various liver and renal diseases). The device is intended to be used on automated chemistry analyzers in clinical laboratories.
3. Special conditions for use statement(s): For prescription use only.

4. Special instrument requirements:

The applicant performed studies using the Hitachi 917 and provided application parameters in the labeling for the Hitachi 911 and Hitachi 717.

I. Device Description:

The LDL-EX SEIKEN Assay kit is an in vitro diagnostic test for the quantitative determination of low density lipoprotein cholesterol (LDL-C) in human serum and heparinized or EDTA plasma on automated chemistry analyzers in clinical laboratories.

The LDL-EX SEIKEN Assay kit includes two working solutions R1 and R2 and a lyophilized Lipid Calibrator for reconstitution with 1.0 ml of distilled water.

The LDL-EX SEIKEN Assay kit Lipid Calibrator is a preparation of lyophilized human serum containing various lipoproteins including LDL. Each serum donor unit has been tested by FDA-approved methods and found negative for Hepatitis B surface antigen (HBsAg), antibody to HCV, and antibody to HIV using FDA approved methods.

J. Substantial Equivalence Information:

1. Predicate device name(s): N-Geneous LDL Cholesterol Reagent
2. Predicate 510(k) number(s): k971573
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	Used for the determination of LDL-C	Used for the determination of LDL-C
Method	Homogenous method to determine LDL-C in serum or plasma directly	Homogenous method to determine LDL-C in serum or plasma directly

Differences		
Item	Device	Predicate
Conjugated and unconjugated bilirubin interference	Up to 60mg/dL	Up to 20 mg/dL

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

The Denka Seiken LDL-EX Assay Kit was certified by the Cholesterol Reference Method Laboratory Network (CRMLN) as meeting the National Cholesterol Program's (NCEP) performance criteria for accuracy and precision on the Hitachi 717.

L. Test Principle:

The assay consists of two steps and is based on the technique to use well-characterized surfactants that react with certain groups of lipoproteins. In the first step, non-LDL lipoproteins, that is chylomicrons, VLDL, IDL and HDL are decomposed by surfactant in Reagent 1 that is reactive to these non-LDL lipoproteins. The cholesterol released from such non-LDL lipoproteins is then degraded to water and oxygen by enzymatic action. Cholesterol ester is hydrolyzed and then oxidized by cholesterol oxidase.

In the second step, another surfactant from reagent 2 releases cholesterol from the LDL-C particles and cholesterol released from LDL is subjected to enzymatic reactions. Hydrogen peroxide produced from the reaction of cholesterol esterase and cholesterol oxidase develops a purple-red color with the coupler in the presence of peroxidase.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Both within and between run studies were performed using three levels of control material using the Hitachi 917 analyzer.

Within-run

	Low Level	Mid Level	High Level
N	20	20	20
Mean (mg/dL)	70.6	123.6	172.2
SD (mg/dL)	0.50	0.66	1.00
CV%	0.70	0.53	0.58

Between-run

	Low Level	Mid Level	High Level
N	40	40	40
Mean (mg/dL)	71.6	122.9	174.2
SD (mg/dL)	1.17	1.43	1.70
CV%	1.63	1.17	0.97

b. Linearity/assay reportable range:

The primary assay range is 1 – 800 mg/dL. The linearity was assessed using equally spaced serial dilutions of serum based high and low controls spiked with purified human LDL. The serial dilutions of the control sera were prepared using saline as the diluent. Comparison of the observed concentrations with the theoretical concentrations showed bias within plus or minus 5% at least up to 800mg/dL.

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

The LDL-EX SEIKEN Assay kit Lipid Calibrator is a preparation of lyophilized human serum containing various lipoproteins including LDL.

LDL-C value is assigned to the Lipid Calibrator with multi lots of the proposed device and with the Primary Serum Calibrator. The Primary Serum Calibrator is a preparation of well-characterized serum pool that is assigned its LDL-C value by ultracentrifugation.

The Lipid Calibrator is stable for 5 days at 2 to 10°C after reconstitution. Once reconstituted, freezing is not recommended.

d. Detection limit:

The Analytical Sensitivity (lower detection limit) was assessed using zero standard (saline) and serial dilutions of in-house control serum. All the samples were assayed in 10 replicates and a mean value and SD were calculated for each sample. The Analytical Sensitivity (lower detection limit) was determined as LDL-C concentration of which mean $-2.6SD$ does not overlap with the mean of $+2.6SD$ of the zero standard (saline). The lower detection limit was established as 0.6mg/dL.

e. Analytical specificity:

Hemoglobin (up to 1000mg/dL), conjugated bilirubin (up to 60mg/dL), unconjugated bilirubin (up to 60mg/dL), or ascorbic acid (up to 50 mg/dL) do not interfere with the assay. When purified VLDL fraction was spiked to a base serum to test triglyceride interference, no significant interference was observed up to 1000 mg/dL triglyceride concentration.

f. Assay cut-off: N/A

2. Comparison studies:

a. *Method comparison with predicate device:*

The Denka Seiken LDL-EX Assay Kit was compared to a commercially available homogenous method using 100 male and female human samples ranging from 42.2 to 195.6 mg/dL. The linear regression analysis showed $Y = 0.982X + 1.83$ $r=0.994$.

Additionally, The Denka Seiken LDL-EX Assay Kit was certified by the Cholesterol Reference Method Laboratory Network (CRMLN) as meeting the National Cholesterol Program's (NCEP) performance criteria for accuracy and precision using the Hitachi 717 analyzer.

b. *Matrix comparison:*

To demonstrate equivalence of the Denka Seiken LDL-EX SEIKEN Assay Kit results in serum and plasma samples, comparison studies were performed in serum samples compared to Heparin and EDTA plasma samples.

Plasma tubes used : Heparin – BD Vacutainer LH PST (Heparin-Li)
EDTA – TERUMO(EDTA-2Na)

Correlation : Hepranized Plasma $Y = 0.972X + 1.474$, $R^2 = 0.999$
EDTA Plasma $Y = 0.964X + 1.797$, $R^2 = 0.998$

3. Clinical studies:

a. *Clinical Sensitivity:* N/A

b. *Clinical specificity:* N/A

c. Other clinical supportive data (when a. and b. are not applicable): N/A

4. Clinical cut-off: N/A

5. Expected values/Reference range:

LDL cholesterol distribution in apparently healthy adults, 181 healthy men with age distribution of 19 – 63 years (mean 38.8 years) and 183 women with age distribution of 18 – 58 years (mean 37.3 years), was studied with the LDL-EX SEIKEN Assay Kit. The expected values for serum LDL-C were found as follows:

Males: 67 – 173 mg/dL
Females: 67 – 163 mg/dL

The Adult Treatment Panel (ATP) III of the National Cholesterol Education Program (NCEP) defines LDL-C as the primary target of therapy and sets five classification categories shown below.

<u>LDL-C Level</u>	<u>Classification</u>
<100 mg/dL	Optimal
100 - 129 mg/dL	Near optimal/above optimal
130 - 159 mg/dL	Borderline High
160 - 189 mg/dL	High
≥ 190 mg/dL	Very High

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.