December 22, 2022

SENTINEL CH. S.p.A.
Patricia Dupé
Head of Quality System
Via Robert Koch 2
Milan, 20152
Italy

Re: K211058
Trade/Device Name: Lp(a) Ultra
Regulation Number: 21 CFR 866.5600
Regulation Name: Low-Density Lipoprotein Immunological Test System
Regulatory Class: Class II
Product Code: DFC
Dated: August 5, 2022
Received: August 5, 2022

Dear Patricia Dupé:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Paula Caposino -S

Digitally signed by Paula Caposino -S
Date: 2022.12.22 14:46:20 -05'00'

Paula Caposino, Ph.D.
Acting Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
k211058

Device Name
Lp(a) Ultra

Indications for Use *(Describe)*
The Lp(a) Ultra assay is intended for in vitro diagnostic use in the immunoturbidimetric quantitative determination of lipoprotein (a) [Lp(a)] in human serum and plasma using an automated analyzer. The measurement of Lp(a) is useful in evaluating lipid metabolism disorders and assessing atherosclerotic cardiovascular disease in specific populations, when used in conjunction with clinical evaluation.
For In Vitro Diagnostic use.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) SUMMARY

1. Applicant Name

SENTINEL CH. S.p.A.
Via Robert Koch, 2
Milano (MI)
20152, Italy
+39 02 345 514 1

Primary contact person for all communications:

Patricia Dupé
Head of Quality System
Phone: +39 02 34 551 496
Fax: +39 02 34 551 464
Email: patriciadupe@sentinel.it

2. Device Name and Classification

Trade name: Lp(a) Ultra
Device Classification: Class II
Regulation: 21CFR 866.5600
Regulation Name: Low-density lipoprotein immunological test system
Product Code: DFC
Device Name: Lipoprotein, Low-Density, Antigen, Antiserum, Control
Medical Specialty: Immunology

3. Predicate Device

Diazyme Lipoprotein (a) Assay (k180074)

4. Indications for Use

The Lp(a) Ultra assay is intended for in vitro diagnostic use in the immunoturbidimetric quantitative determination of lipoprotein (a) [Lp(a)] in human serum and plasma using an automated analyzer. The measurement of Lp(a) is useful in evaluating lipid metabolism disorders and assessing atherosclerotic cardiovascular disease in specific populations, when used in conjunction with clinical evaluation.
For In Vitro Diagnostic use.

5. Intended Use

The Lp(a) Ultra assay is intended for in vitro diagnostic use in the immunoturbidimetric quantitative determination of lipoprotein (a) [Lp(a)] in human serum and plasma using an automated analyzer.
The measurement of Lp(a) is useful in evaluating lipid metabolism disorders and assessing atherosclerotic cardiovascular disease in specific populations, when used in conjunction with clinical evaluation.
For In Vitro Diagnostic use.

6. Description

Lp(a) Ultra assay is composed by 2 ready to use liquid reagents (Reagent 1and Reagent 2) that are supplied in the following configuration: Reagent 1 fill volume 18 mL in a 20 mL wedge and Reagent 2 fill volume 9 mL in a 20 mL wedge, 1 wedge of each/kit.
The kit contains one plastic (HDPE) vial of Reagent 1 and one plastic (HDPE) vial of Reagent 2, which allows the customer to perform 86 tests (on AU680 automatic analyzer).

7. Principles of the Procedure

Lp(a) Ultra is a latex-based immunoturbidimetric assay developed to measure Lp(a) levels in serum and plasma.
When an antigen-antibody reaction occurs between Lp(a) in a sample and anti-Lp(a) antibody which has been adsorbed to latex particles, agglutination results. This agglutination is detected as an absorbance change, with the magnitude of the change being proportional to the quantity of Lp(a) contained in the sample.

8. Comparison with Predicate Device

The comparison between Lp(a) Ultra and the predicate device Diazyme Lipoprotein (a) Assay is reported in Table 8.1.

Table 8.1. Comparison Lp(a) Ultra vs. Predicate Device Diazyme Lipoprotein (a) Assay

Characteristics	Subject Device Lp(a) Ultra	Predicate Device k180074 Diazyme Lipoprotein (a) Assay
Technical Characteristics		
Classification	Regulation Description: Low-density lipoprotein immunological test system	Same
Method Principle	Quantitative immunoturbidimetric assay	Same
Intended Use	The Lp(a) assay is intended for in vitro diagnostic use in the immunoturbidimetric quantitative determination of lipoprotein (a) [Lp(a)] in human serum and plasma using an automated analyzer. The measurement of Lp(a) is useful in evaluating lipid metabolism disorders and assessing atherosclerotic cardiovascular disease in specific populations, when used in conjunction with clinical evaluation. For In Vitro Diagnostic use.	The Diazyme Lipoprotein (a) Assay is intended as a latex particle enhanced immunoturbidimetric assay for the in vitro quantitative determination of Lipoprotein (a) [Lp(a)] concentration in human serum or plasma on Clinical Chemistry Systems. The measurement of Lipoprotein (a) is useful in evaluating lipid metabolism disorders and assessing atherosclerotic cardiovascular diseases in specific populations, when used in conjunction with clinical evaluation. For *in vitro* diagnostic use only.
Analyte Measured	Lipoprotein (a)	Same
Instrument Used	Beckman Coulter AU680	Ortho Clinical Diagnostics VITROS 4600
Measurement	Quantitative	Same
Specimen Type	Serum, plasma (Na-heparin, Li-heparin, K_2-EDTA, K_3-EDTA)	Serum, plasma (Li-Heparin, K_2EDTA)
Reference Values	Lp(a) < 30 mg/dL	10 mg/dL < Lp(a) < 30 mg/dL
Reagents	Two reagents	Same
Format	Liquid	Same

Characteristics	**Subject Device** **Lp(a) Ultra**	**Predicate Device k180074** **Diazyme Lipoprotein (a) Assay**
Analytical Measuring Range	10 - 100 mg/dL	5.4 - 100 mg/dL
Performance Characteristics		
Storage Temperature	2-8°C	Same
Use of Calibrators	Yes	Same
Use of Controls	Yes	Same

9. PERFORMANCE TESTING SUMMARY

All performance were established using the Beckman Coulter AU680 analyzer.

9.1. Precision (Repeatability/Reproducibility)

9.1.1. Inter-Assay Precision (Total Imprecision)

The Inter-Assay Precision study verifies the agreement between indications or measured quantity values obtained by replicates measurements on the same or similar objects under specified conditions.

The precision was determined on the basis of CLSI EP05-A3 Guideline (Evaluation of Precision of Quantitative Measurement Procedures).

Five samples were used at different concentration ranging from 20 mg/dL to 100 mg/dL. After calibration at Time zero, 2 replicates of each sample were performed on 2 different runs for day. The assay was calibrated at Time 0 and day 15. The procedure was repeated for 28 testing days.

9.1.1.1. Results

A summary of the results is presented in Table 9.1.1.

Table 9.1.1. Inter-Assay Precision Results

Reagent	Material	Total %CV
Lot 90530	Level 1	4.6%
	Level 2	3.2%
	Level 3	5.3%
	Level 4	3.3%
	Level 5	2.3%

The data show good precision across the concentration range from 20 to 100 mg/dL.

9.1.2. Intra-Assay Precision (Within Run)

The Intra-Assay Precision study verifies the precision and the trueness of the method relative to the assigned values of materials with known concentrations.

The Intra-Assay Precision was determined on the basis of CLSI EP15-A3 Guideline (User Verification of Precision and Estimation of Bias).

Five samples were used at different concentration ranging from 20 mg/dL to 100 mg/dL. After calibration, 20 replicates of each sample were run on 3 different runs (each run with a new calibration).

9.1.2.1. Results

A summary of the results is presented in Table 9.1.2.

Table 9.1.2. Intra-Assay Precision Results

Reagent	Run	Material	Concentration mg/dL	Total %CV	SD mg/dL
Lot 90266	1	Level 1	19.0	3.5	0.7
		Level 2	47.0	2.7	1.3
		Level 3	10.6	3.3	0.4
		Level 4	32.7	1.3	0.4
		Level 5	100.9	0.7	0.8
	2	Level 1	18.9	3.7	0.7
		Level 2	45.9	1.9	0.9
		Level 3	10.7	4.8	0.5
		Level 4	32.8	1.5	0.5
		Level 5	97.7	0.5	0.5
	3	Level 1	19.1	2.8	0.5
		Level 2	46.0	1.1	0.5
		Level 3	11.1	4.4	0.5
		Level 4	33.6	1.6	0.5
		Level 5	99.4	0.8	0.8

All the calculated CV% are lower than 5%.

9.2. Linearity

9.2.1. Linearity - Analytical Measuring Range

The study was performed to establish the Upper Limit of Analytical Measurement Range (AMR) based upon the linearity of the Lp(a) assay on Beckman Coulter AU680.

Linearity was evaluated using guideline CLSI EP06 (Evaluation of the Linearity of Quantitative Measurement Procedures, 2nd Edition

9.2.1.1. Results

A summary of the results is presented in Table 9.2.1.

Table 9.2.1. Linearity Results

Reagent	Tested range (mg/dL)	Range found as Linear (mg/dL)
Lot 00507	1.0 to 139.0	8.4 to 105.5
Lot 10208	1.2 to 131.5	8.4 to 103.8

The results demonstrate that the assay is linear up to 100 mg/dL. The upper limit of the AMR is 100 mg/dL.
The AMR is claimed as 10 mg/dL to 100 mg/dL as resulted from sensitivity (LoQ) and from linearity studies.

9.3. Analytical Sensitivity/Detection Limit

9.3.1. Limit of Blank (LoB) Study

The Limit of Blank (LoB) study was performed to determine the highest measurement result that is likely to be observed (with a stated probability) for a blank sample.
The LoB study was performed using the guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP17-A2
For two different reagent lots, 4 saline samples (zero-analyte samples) were tested in 5 replicates in three different runs, for a total of 60 measurements for each lot.

9.3.1.1. Results

A summary of the results is presented in Table 9.3.1.

Table 9.3.1. Limit of Blank Results

Reagent	Limit of Blank (LoB) mg/dL
Lot 90266	0.7
Lot 90530	0.7

The observed Limit of Blank supports the LoB claim of 0.7 mg/dL.

9.3.2. Limit of Detection (LoD) Study

The Limit of Detection (LoD) is the lowest analyte concentration likely to be reliably distinguished from the LoB and at which detection is feasible.

The LoD was determined on the basis of CLSI EP17-A2 Guideline (Evaluation of detection capability for clinical laboratory measurement procedures).

9.3.2.1. Results

A summary of the results is presented in Table 9.3.2.

Table 9.3.2. Limit of Detection Results

Reagent	Limit of Detection (LoD) mg/dL
90266	1.6
90530	1.9

The Limit of Detection is chosen to be the highest value obtained. The LoD value observed supports the claim of 1.9 mg/dL.

9.3.3. Limit of Quantitation (LoQ) Study

The Limit of Quantitation (LoQ) is the lowest amount of a measure and in a material that can be quantitatively determined with stated accuracy (as total error or as independent requirements for bias and precision), under stated experimental conditions.

The LoQ was determined on the basis of CLSI EP17-A2 Guideline (Evaluation of detection capability for clinical laboratory measurement procedures).

9.3.3.1. Results

A summary of the results is presented in Table 9.3.3.

Table 9.3.3. Limit of Quantitation Results

Reagent	Limit of Quantification (LoQ) mg/dL
Lot 90266	2.5
Lot 90530	3.0

The LoQ observed supports the claim of 3.0 mg/dL.

9.4. Interference

9.4.1. Endogenous Interferences Study

The Interferences Study was performed to evaluate the influence some endogenous substance on the performances of the product.

The study was performed on the basis of EP07 3rd Edition – Interference Testing in Clinical Chemistry.

The interference was evaluated at the following Lp(a) concentrations:

Low: ≈ 30 mg/dL

High: ≈ 50 mg/dL

For each concentration 2 aliquots of serum pool were prepared:

- 1st aliquot: Test Sample (High Test Sample)
- 2nd aliquot: Control Sample (Low Test Sample)

The study was divided in two procedures:

1) Paired Difference Tests

   Test Sample and Control Sample were tested in different replicates. If there is no interferences the study was concluded. If Interference is confirmed, proceed with the 'Interference test'

2) Interference test

   The Test Sample aliquots were diluted using the Control Sample to obtain additional dilution levels in the ratio ranging from 100% to 0%

9.4.1.1. Results

A summary of the results is presented in Table 9.4.1.

Table 9.4.1. Interferences Results Summary

Interfering substance	**Tested concentration up to**	**Observed concentration without Interferences Pool Low**	**Observed concentration without Interferences Pool High**
Intralipid® Sterile Fat Emulsion	1000 mg/dL	1000 mg/dL	1000 mg/dL
Triglycerides	1000 mg/dL	715 mg/dL *	
Conjugated bilirubin	60 mg/dL	60 mg/dL	60 mg/dL
Unconjugated bilirubin	60 mg/dL	60 mg/dL	60 mg/dL
Rheumatoid Factor	500 UI/mL	500 UI/mL	500 UI/mL
Hemoglobin	1000 mg/dL	1000 mg/dL	1000 mg/dL
Ascorbic Acid	180 mg/dL	180 mg/dL	180 mg/dL

* Triglycerides was tested in patient serum samples without significant interference at triglycerides concentration ranging from 461 to 715 mg/dL.

9.5. Stability

9.5.1. On Board Calibration Study

The Stability study allows to verify the On Board and the Calibration Stability of the product.

The On Board and the Calibration Stability were determined on the basis of CLSI EP25-A Guideline (Evaluation of Stability of in Vitro Diagnostics Reagents).

For the study, 5 samples were used at different concentration ranging from 20 mg/dL to 100 mg/dl.

9.5.1.1. Results

A summary of the results is presented in Table 9.5.1.

Table 9.5.1. On Board Calibration Results

Reagent	Material	%bias Min	% bias Max
Lot 90530	Level 1	-2.7%	5.1%
	Level 2	-0.7%	1.4%
	Level 3	-4.8%	0.7%
	Level 4	-3.4%	1.0%
	Level 5	-1.3%	1.1%

The Calibration Stability claim is 15 days on the AU 680 Analyzer. The on-board stability claim is 30 days on the AU680 analyzer.

9.6. Other Analytical Performance

9.6.1. Prozone Study

The High Dose Hook Effect (Prozone) study was performed to determine the analyte concentration at which false negatives results may occur.

For the study, the last calibrator level of calibrator set reconstituted with 191 µL was used to reach a high concentration (approx. 500.0 mg/dL).

The sample was diluted in saline to obtain some concentration points within the analytical measuring range.

9.6.1.1. Results

No Prozone effect was observed up to concentration of 500.0 mg/dL. No prozone effect up to the upper limit of the measuring range is claimed.

9.7. Comparison Studies

9.7.1. Method Comparison vs. Predicate Device

Purpose of this study is to evaluate the performances of Lp(a) Ultra assay on Beckman Coulter AU680 Analyzer, compared to the predicate device Diazyme® Lipoprotein (a), REF DZ131B-K, on VITROS® 4600, Ortho Clinical Diagnostics.

The method comparison study was performed based on guidance from the CLSI document EP09c 3rd Edition.

9.7.1.1. Results

A summary of the results is presented in Table 9.7.1.

Table 9.7.1. Method Comparison vs. Predicate Device Results

	Results - Passing & Bablok fit	**Results - Linear fit-**
r	0.995	0.995
Slope	0.9850 (0.9706 – 1.0000)	0.9771 (0.9612 – 0.9929)

9.7.2. Matrix Comparison – Lithium Heparin

This study was performed to demonstrate correlation between Serum samples and Plasma Lithium Heparin samples.

The Matrix Comparison study was performed based on guidance from the CLSI document EP09c 3rd Edition.

57 serum and Lithium Heparin plasma samples, derived from the same patients were tested in duplicate.

9.7.2.1. Results

A summary of the results is presented in Table 9.7.2.

Table 9.7.2. Matrix Comparison – Lithium Heparin Results

	Results - Passing & Bablok fit -	**Results - Linear fit-**
r	0.997	0.997
Slope	0.99 (0.95 – 1.03)	0.98 (0.95 – 1.00)

9.7.3. Matrix Comparison – Sodium Heparin

This study was performed to demonstrate correlation between Serum samples and Plasma Sodium Heparin samples.

The method comparison study was performed based on guidance from the CLSI document EP09c 3rd Edition.

58 serum and Sodium Heparin plasma samples, derived from the same patients were tested in duplicate.

9.7.3.1. Results

A summary of the results is presented in Table 9.7.3.

Table 9.7.3. Matrix Comparison – Sodium Heparin Results

	Results - Passing & Bablok fit -	**Results - Linear fit-**
r	0.999	0.999
Slope	0.99 (0.95 – 1.01)	0.99 (0.97 – 1.00)

9.7.4. Matrix Comparison – Di-Potassium EDTA

This study was performed to demonstrate correlation between Serum samples and Plasma Di-Potassium EDTA samples.

The Matrix Comparison study was performed based on guidance from the CLSI document EP09c 3rd Edition.

57 serum and Di-Potassium EDTA plasma samples, derived from the same patients were tested in duplicate.

9.7.4.1. Results

A summary of the results is presented in Table 9.7.4.

Table 9.7.4. Matrix Comparison – Di-Potassium EDTA Results

	Results - Passing & Bablok fit -	**Results - Linear fit-**
r	0.997	0.997
Slope	0.97 (0.95 – 1.01)	0.98 (0.96 – 1.00)

9.7.5. Matrix Comparison - Tri-Potassium EDTA

This study was performed to demonstrate correlation between Serum samples and Plasma Tri-Potassium EDTA samples.

The method comparison study was performed based on guidance from the CLSI document EP09c 3rd Edition.

56 serum and Tri-Potassium EDTA plasma samples, derived from the same patients were tested in duplicate.

9.7.5.1. Results

A summary of the results is presented in Table 9.7.5.

Table 9.7.5. Matrix Comparison – Tri-Potassium EDTA Results

	Results - Passing & Bablok fit -	**Results - Linear fit-**
r	0.998	0.998
Slope	0.99 (0.95 – 1.03)	0.99 (0.98 – 1.01)

10. CONCLUSIONS

Testing results indicate that the proposed device Lp(a) Ultra is substantially equivalent to the predicate device.