July 19, 2023

numares AG
Stefanie Dukorn
Head of Quality and Regulatory Affairs
Am BioPark 9
D-93053 Regensburg
Germany

Re: K210801
Trade/Device Name: AXINON® LDL-p Test System
Regulation Number: 21 CFR 862.1475
Regulation Name: Lipoprotein Test System
Regulatory Class: Class I, subject to limitations of exemptions per 21 CFR 862.9(c)(4)
Product Code: MRR
Dated: November 18 2022
Received: November 18, 2022

Dear Stefanie Dukorn:

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 V. Caposino
-S

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)*
K210801

Device Name
AXINON® LDL-p Test System

Indications for Use *(Describe)*
The AXINON® LDL-p Test System is intended to measure lipoprotein particles to quantify LDL particle number (LDL-p) using nuclear magnetic resonance (NMR) spectroscopy that measures the 600 MHz proton nuclear magnetic resonance (NMR) spectrum of a human serum sample. LDL-p concentration values are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease. This test system is for professional use only.

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

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. The assigned 510(k) number is K210801.

807.92 (a)(1): Name: numares AG
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807.92 (a)(2): Device name- trade name and common name, and classification

Trade name: *AXINON® LDL-p Test System*

Common Name: *AXINON® LDL-p Test System*

Classification Names:
Lipoprotein test system, 21 CFR 862.1475, Product Code MRR

807.92 (a)(3): Identification of the legally marketed predicate devices

The *AXINON® LDL-p Test System* is substantially equivalent to the NMR Lipoprofile Assay (K063841).

807.92 (a)(4): Device Description

The *AXINON® LDL-p Test System* involves measurement of the 600 MHz proton NMR spectrum of a serum sample, deconvolution of the composite signal at approximately 0.85 ppm to produce signal amplitudes of lipoprotein subclass proportions that contribute to the composite serum signal, and conversion of these subclass signal amplitudes to lipoprotein subclass concentrations. The 0.85 ppm serum NMR signal arises mainly from the methyl group protons of the lipids carried in the VLDL, LDL and HDL subclasses of varying diameters. The NMR signals from the various lipids within the lipoprotein subclasses have unique and distinctive shapes and frequencies, uncovered by the granular decomposition of the composite serum signal. Each of these lipid signal representatives is proportional to the number of subclass particles emitting the signal, which enables subclass particle concentrations to be calculated from the subclass signal amplitudes derived from the spectral deconvolution analysis. LDL subclass particle concentrations, in units of nanomoles of particles per liter (nmol/L), are summed to give the reported total LDL particle concentration (LDL-p).

The AXINON® LDL-p Test System including the *AXINON® Analyzer* is a clinical laboratory analyzer that employs nuclear magnetic resonance spectroscopic detection to quantify multiple analytes in biological fluid specimens, specifically human serum.
The *AXINON® Analyzer* system is distributed across two separate computers:
The workstation running *AXINON® Software* is the main host of the system. It controls user interfaces, data handling, results calculation, schedules and manages all activities required to process a sample, and manages remote access to the NMR system.
In addition, *AXINON® Analyzer* comes with the optional software utility *AXINON® Sample Wizard* that supports manual sample preparation procedures.
The NMR workstation controls all magnet operations and the hardware in the sample handler.

807.92 (a)(5): Intended Use

The *AXINON® LDL-p Test System* is intended to measure lipoprotein particles to quantify LDL particle number (LDL-p) using nuclear magnetic resonance (NMR) spectroscopy that measures the 600 MHz proton nuclear magnetic resonance (NMR) spectrum of a human serum sample. LDL-p concentration values are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease. This test system is for professional use only.

807.92 (a)(6): Technological Similarities and Differences to the Predicate

The *AXINON® LDL-p Test System* is as safe and effective as the predicate device, K063841**.**
The minor technological differences between the *AXINON® LDL-p Test System* and the predicate device (spectrometer frequency) raise no new issues of safety or effectiveness. The restriction of AXINON® LDL-p to a single output parameter (without HD-C and Triglycerides) does not raise new issues of safety of effectiveness, as these are readily available in routine diagnostic and all results are used in conjunction with other lipid measurements and clinical evaluation.

Comparison with predicate

	Predicate NMR Lipoprofile-2 Assay and NMR Profiler Test System	**Proposed *AXINON® LDL-p Test System***
510(k) number	K063841	K210801
Intended Use / Indications for Use	The NMR LipoProfile® -2 test, used with the NMR Profiler, an automated NMR spectrometer, measures lipoprotein particles to quantify LDL particle number (LDL-P), HDL cholesterol (HDL-C), and triglycerides in serum and plasma using nuclear magnetic resonance (NMR) spectroscopy. LDL-P and these NMR-derived concentrations of triglycerides and HDL-C are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease. This test is performed and provided as a service by LipoScience Laboratory.	The AXINON® LDL-p Test System is intended to measure lipoprotein particles to quantify LDL particle number (LDL-p) using nuclear magnetic resonance (NMR) spectroscopy that measures the 600 MHz proton nuclear magnetic resonance (NMR) spectrum of a human serum sample. LDL-p concentration values are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease. This test system is for professional use only.
Technology	Nuclear magnetic resonance	Same
Multi- analyte	No	Same
Detection Method	400 MHz proton NMR spectrum	600 MHz proton NMR spectrum
Data Acquisition Software	Possess data acquisition software and software to process detected signals	Same
Patient Population	General	Same
Instrument Platform	NMR profiler	*AXINON®* Analyzer
Specimen	Human serum and plasma	Human serum
Analyzer	400 MHz NMR Spectrometer	600 MHz NMR Spectrometer
Spectral Deconvolution Computational Processes	Linear least-squares with singular value decomposition of the spectra from each specimen	Similar
Reference Range	Distribution of LDL-p observed in a general apparently healthy population of men and women	Same

We performed analytical validations to demonstrate that the *AXINON® LDL-p test system* is equivalent to the *NMR LipoProfile®* test on the Vantera Clinical Analyzer. The comparative analytical performance is shown in tables below.

LDL-p		***AXINON® LDL-p Test System***						**Predicate Device**	
Detection capability									
LoB		0 nmol/L						n.d.	
LoD		99 nmol/L						n.d.	
LoQ		139.7 nmol/L						300 nmol/L	
Measuring range		300 – 3100 nmol/L						300 - 3500 nmol/L	
Linearity regression		y = 1.05x - 28.33						n.d.	
Linearity R^2		0.998						n.d.	
Within-run precision (Repeatability)		**LV 1**	**LV 2**	**LV 3**	**LV 4**	**LV 5**	**LV 6**	**LV 1**	**LV 2**
Mean	Lot1	653.8	1006.8	1069.0	1098.0	1424.9	2857.3	2222	1042
	Lot2	674.2	1026.3	1081.6	1117.0	1474.5	2909.5		
	Lot3	656.2	1001.2	1065.9	1105.2	1447.8	2875.4		
SD	Lot1	14.88	20.34	22.54	16.95	24.28	35.76	49,1	47.7
	Lot2	21.51	22.95	23.16	22.07	23.41	33.02		
	Lot3	21.33	21.25	20.92	24.04	23.93	28.61		
CV %	Lot1	2.28	2.02	2.11	1.54	1.70	1.25	2.2%	4.6%
	Lot2	3.19	2.24	2.14	1.98	1.59	1.13		
	Lot3	3.25	2.12	1.96	2.18	1.65	0.99		
Within-lab Precision		**LV 1**	**LV 2**	**LV 3**	**LV 4**	**LV 5**	**LV 6**	**LV 1**	**LV 2**
Mean	Lot1	653.8	1006.8	1069.0	1098.0	1424.9	2857.3	1925	1053
	Lot2	674.2	1026.3	1081.6	1117.0	1474.5	2909.5		
	Lot3	656.2	1001.2	1065.9	1105.2	1447.8	2875.4		
SD	Lot1	29.16	32.93	36.75	33.37	37.17	116.15	66.7	68.4
	Lot2	36.26	31.72	38.22	34.22	39.67	104.63		
	Lot3	34.22	40.14	32.28	40.39	45.41	112.62		
CV%	Lot1	4.46	3.27	3.44	3.04	2.61	4.07	3.5%	6.5%
	Lot2	5.38	3.09	3.53	3.06	2.69	3.60		
	Lot3	5.22	4.01	3.03	3.65	3.14	3.92		
Method comparison		Linear regression y = 1.07x -90.16, R=0.955						clinical	
Interference study		10 Endogenous and 26 Exogenous were tested. Naproxen (sodium salt) at above 0.55 mmol/L may cause falsely low results. 1-propanol at concentrations above 1 mmol/L may cause missing or falsely low results.						5 Endogenous and 20 Exogenous were tested.	
Specimen stability		Prepared serum: Refrigerated Stability 5 days						NMR Lipotube: freshly draw serum	

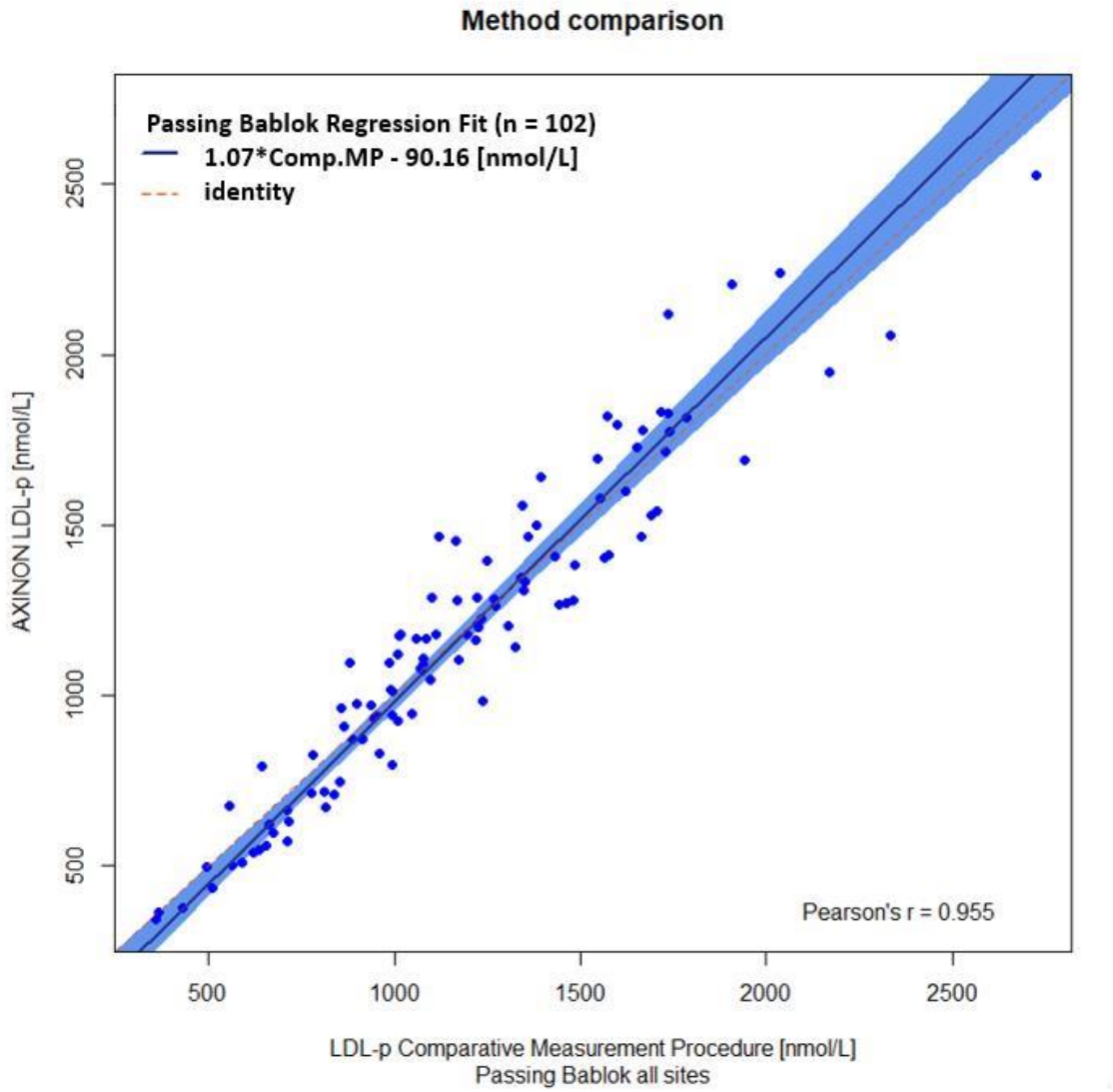
807.92 (b)(1): Brief Description of Nonclinical Data

Linearity: For LDL-p, the measurement procedure shows linearity for the interval from 300 to 3100 nmol/L, with deviations from linearity within ± 10% for the range from 800 nmol/L to 3100 nmol/L and within ± 80 nmol/L for the range from 300 nmol/L to 800 nmol/L. In a study with 11 levels and five replicates for each level, the maximum observed % deviation from linearity was 23.2% (at 219 nmol/L) and the maximum observed absolute deviation was 126.7 nmol/L (at 3285 nmol/L).

Precision: within-run imprecision and within-lab precision were determined at six concentration levels, measured in duplicates in two runs each day over a period of 20 days with three lots of reagents.

Sample ID (Description)	lot	Mean Value	N	Repeatability		Between-Run		Between-Day		Within-Laboratory	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV
Pool2 (pooled patient samples)	1	653.8	80	14.88	2.28	25.07	3.83	0	0	29.16	4.46
	2	674.2	80	21.51	3.19	29.19	4.33	0	0	36.26	5.38
	3	656.2	80	21.33	3.25	26.76	4.08	0	0	34.22	5.22
Pool 4 (pooled patient samples)	1	1006.8	80	20.34	2.02	22.35	2.22	13.09	1.30	32.93	3.27
	2	1026.3	80	22.95	2.24	9.63	0.94	19.67	1.92	31.72	3.09
	3	1001.2	80	21.25	2.12	32.20	3.21	11.06	1.10	40.14	4.01
Pool 3 (pooled patient samples)	1	1069.0	80	22.54	2.11	25.71	2.41	13.47	1.26	36.75	3.44
	2	1081.6	80	23.16	2.14	21.72	2.01	21.28	1.97	38.22	3.53
	3	1065.9	80	20.92	1.96	20.84	1.95	13.05	1.22	32.28	3.03
Pool 1 (pooled patient samples)	1	1098.0	80	16.95	1.54	23.98	2.18	15.85	1.44	33.37	3.04
	2	1117.0	80	22.07	1.98	16.70	1.50	20.13	1.80	34.22	3.06
	3	1105.2	80	24.04	2.18	23.42	2.12	22.47	2.03	40.39	3.65
Pool 5 (pooled patient samples)	1	1424.9	80	24.28	1.70	22.35	1.57	17.12	1.20	37.17	2.61
	2	1474.5	80	23.41	1.59	24.86	1.69	20.19	1.37	39.67	2.69
	3	1447.8	80	23.93	1.65	25.72	1.78	28.78	1.99	45.41	3.14
Pool 6 (commercial control)	1	2857.3	80	35.76	1.25	33.29	1.17	105.38	3.69	116.15	4.07
	2	2909.5	80	33.02	1.13	47.33	1.63	87.28	3.00	104.63	3.60
	3	2875.4	80	28.61	0.99	55.11	1.92	93.96	3.27	112.62	3.92

Method comparison: The experiment was performed on 102 samples from volunteers against the comparative method distributed over three different sites. Passing-Bablok regression slopes were found to deviate less than 15% from 1.0 for all sites (1.12, 0.99, 1.06; combined 1.07). The estimated mean relative bias with respect to the comparative method was found to be -1.04% overall and -2.14%, -0.99% and 0.01% for the different sites, respectively. The estimated mean relative bias therefore lies well within the (optional) acceptance criterion of < 10%. All observed values covered the claimed measuring range. No data was found to be missing.



Limit of quantification: The experiment was performed on a single instrument with three lots of reagents; 20 replicates from 4 different serum pools of low concentration were measured within 3 days. The lowest concentration that still meets the total CV of < 20% over all batches is 139.7 nmol/l, representing the limit of quantification.
Limit of blank and limit of detection: The limit of blank and limit of detection was determined according to an internal protocol on the basis of guideline CLSI EP17-A2. The limit of blank is zero and was confirmed by testing of 30 samples with three lots of reagents. The limit of detection was determined using the probit approach. The experiment was performed with two lots of reagents. Three sample pools were measured in eight dilution levels per pool in replicates of seven over three days. The limit of detection is 99.1 nmol/l.

Interfering substances: Two human serum specimens with different LDL-p concentrations were tested for each substance in five replicates each with a single lot of reagents on a single device. Criterion: Recovery within ± 10 % of initial value.
Naproxen (sodium salt) at above 541 µmol/L may cause falsely low results (up to -14.11%).
1-propanol at concentrations above 1 mmol/L may cause missing or falsely low results.

Traceability, Stability, Assigned values (controls, calibrators)

AXINON® Serum Calibrator (NMR instrument calibration)

The *AXINON®* Serum Calibrator (containing Maleic Acid as Sodium salt), is used as the NMR calibrator for the *AXINON® Analyzer*. *AXINON®* Serum Calibrator is used routinely as a calibrator once per measured rack during measurement startup to establish current normalization factors in each analytical run. It also serves as one quality assessment tool to ensure quality NMR spectra are produced by the NMR analyzer.
The stability of *AXINON®* Serum Calibrator under recommended storage conditions was evaluated for a period of more than 36 months. It was stored refrigerated at 2-10°C, in its primary packaging. *AXINON®* Serum Calibrator samples were evaluated for maleic acid signal integrals regularly during the observation period. The *AXINON®* Serum Calibrator is stable for 12 months in the primary packaging at the recommended refrigerated storage conditions. To assign values, 15 samples of a new lot of *AXINON®* Serum Calibrator are measured using 15 samples of a certified reference material as master calibrator. Means, Standard Deviations and % CVs are computed and values are assigned.

AXINON® Serum Control

The *AXINON®* Serum Control is used as the NMR control (comprising Acetic Acid as Sodium salt) for the *AXINON® Analyzer*. *AXINON®* Serum Control is used routinely as a quality control material once per measured rack during measurement startup and termination to verify current normalization factors in each analytical run. It also serves as second quality assessment tool to ensure quality NMR spectra are produced by the NMR analyzer.
The stability of *AXINON®* Serum Control under recommended storage conditions was evaluated for a period of more than 24 months. It was stored refrigerated at 2-10°C, in its primary packaging. *AXINON®* Serum Control samples were evaluated for Acetic acid concentration regularly during the observation period. The *AXINON®* Serum Control is stable for 12 months in the primary packaging at the recommended refrigerated storage conditions. To assign values, 30 samples of a new lot of *AXINON®* Serum Control are run in house on three different runs using standard calibration procedures. Means, Standard Deviations and % CVs are computed, and values are assigned.

External Controls

Bio-Rad LIQUID ASSAYED MULTIQUAL is frozen human serum-based control material available in three levels, prepared and packaged by Bio-Rad Laboratories.

It is recommended that two levels of quality control materials are tested in the same manner as patient samples, before or during patient sample processing for each analyte being tested. To verify system performance, analyze control materials:

- After calibration
- According to federal, state or local regulations or at least once every day when patient testing is being performed.

It is recommended that each laboratory establish its own mean and acceptance range for each new lot of controls. Patient results should not be reported if the Quality Control values are not within the expected range.

807.92b)(2): Brief Description of Clinical Data

a. Clinical Sensitivity:
Not Applicable

b. Clinical specificity:

Not Applicable

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

Not Applicable

1. Clinical cut-off:

Not Applicable

2. Expected values: In order to confirm the distribution of LDL-p values measured with AXINON Serum Kit 2.0 and AXINON LDL-p with AXINON Analyzer 1.0, 40 serum samples from apparently healthy subjects (20 men, 20 women, residents in the United States) were analyzed. No outliers were detected by the Tukey method (1977). The reference interval was determined according to an internal protocol on the basis of guideline CLSI EP28-A3C by transference from the interval determined by Matyus et al., Clinical Biochemistry 47 (2014) 203–210.
The reference interval for LDL-p is 542 – 1986 nmol/L for women, and 528 – 2169 nmol/L for men, being the central 90% of values (at the 5th and 95th percentiles).
Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary, determine its own reference ranges.

807.92 (b)(3): Conclusions from Nonclinical and Clinical Data
The conclusions drawn from the analytical and clinical data demonstrate that the device is substantially equivalent to the predicate.