K063841

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Raleigh, NC 27616

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510(k) Summary

LipoScience NMR LipoProfile-2 Assay and NMR Profiler Instrument Test System

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.

Assigned 510(k) Number: *K063841*

Submitter's Name, Address, Telephone Number, Contact Person, and Date Prepared

Submitter:
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Date Prepared: September 18, 2006 (summary revised July 17, 2008)

Name of Device and Name/Address of Sponsor

Name of Device
NMR LipoProfile-2 Assay and NMR Profiler Test System

Sponsor:

LipoScience, Incorporated
2500 Sumner Boulevard
Raleigh, NC 27616

Common or Usual Name

NMR LipoProfile test

Classification Name (s)

Lipoprotein test system (21CFR 862.1475, product codes MRR and LBS)
Triglyceride test system (21CFR 862.1705, product code CDT)
Quality control material (21 CFR 862.1660, product code JJY)
Calibrator (21 CFR 862.1150, JIT)

Predicate Device(s)

Device Name: Dimension Automated LDL Cholesterol Flex Reagent
Manufacturer: Dade Behring, Inc.
510(k) Number: K020724

Device Name: Triglycerides Reagent
Manufacturer: Carolina Liquid Chemistries
510(k) Number: K971324

Device Name: Liquid N-geneous HDL Cholesterol Kit
Manufacturer: Genzyme Corporation
510(k) Number: K971162

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.

Device Description

Principle of Operation

The *NMR LipoProfile* Test involves measurement of the 400 MHz proton NMR spectrum of a plasma or serum sample, deconvolution of the composite signal at ~0.8 ppm to produce the signal amplitudes of the lipoprotein subclasses that contribute to the composite plasma signal, and conversion of these subclass signal amplitudes to lipoprotein subclass concentrations. The 0.8 ppm plasma NMR signal arises from the methyl group protons of the lipids carried in the VLDL, LDL, and HDL subclasses of varying diameter. The NMR signals from the various lipoprotein subclasses have unique and distinctive frequencies and lineshapes, each of which are accounted for in the deconvolution analysis model. Each subclass signal amplitude 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). By employing conversion factors that assume that the various lipoprotein subclass particles have cholesterol and triglyceride contents characteristic of normolipidemic individuals, HDL cholesterol and triglyceride concentrations are also derived.

Types of Specimen

Freshly drawn serum collected in an NMR LipoTube is the preferred specimen. Freshly drawn serum collected in plain red-top blood collection tubes and EDTA or heparin plasma are also acceptable specimens. The optimum specimen volume is ≥0.5 mL. Patient fasting is not necessary prior to the blood draw, except for determination of fasting triglyceride concentrations.

Testing Procedure

Each patient specimen is diluted 2-fold using the NMR Diluent, mixed thoroughly, and placed in separate specimen vials in predefined locations of the bar-coded measurement racks. Automated testing is then initiated according to the operating instructions.

Result Calculation

The NMR Profiler test system performs all calculations necessary to produce the final reported results. These calculations include the linear least squares spectral deconvolution analysis which gives the NMR signal amplitudes of each lipoprotein subclass, the conversion of these signal amplitudes to subclass particle concentrations and calculated subclass cholesterol and triglyceride concentrations, and summation of the appropriate subclass concentrations to give the reported values of LDL-P, HDL-C, and triglycerides.

Software and Hardware

The NMR Profiler test system contains a Rack Reader, a Nuclear Magnetic Resonance (NMR) system, and a LipoProfile Analysis Server. These three core systems manage information through databases and file systems. The algorithm resident on the LipoProfile Analysis Server is the foundation of the LipoProfile assay. The NMR system and Rack reader are configured off-the-shelf components. The remaining software serves to transmit data, store data, and report the results of the LipoProfile analysis. The LipoProfiler System may be configured as a stand alone system or integrated into a Laboratory Information System (LIS).

Technological Characteristics and Substantial Equivalence

The NMR LipoProfile test, when used with the NMR Profiler, is as safe and effective as the Dade Dimension Automated LDL Cholesterol Flex Reagent, Carolina Liquid Chemistries Triglycerides Reagent, and Genzyme Liquid N-geneous HDL Cholesterol

test. The NMR LipoProfile test has the same intended uses and similar indications and principles of operation as its predicate devices. The minor technological differences between the NMR LipoProfile test and its predicate devices raise no new issues of safety or effectiveness. Performance data further demonstrate that the NMR LipoProfile test is as safe and effective as its predicate devices. Thus, the NMR LipoProfile test is substantially equivalent.

Similarity to Predicates

As with the predicate assays, the *NMR LipoProfile* test is intended for the separation and quantitation of LDL, HDL, and triglycerides in serum and plasma, measurements of which are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease.

Therefore, substantial equivalence of the NMR LipoProfile Test to the claimed predicate devices is based upon the following:

- substantially similar intended use and indications for use,
- use of the same clinical specimen (serum and plasma)
- substantial similar safety and effectiveness; i.e.; no new questions of safety and effectiveness are raised when the tests are used as intended

Differences from Predicate

The NMR LipoProfile Test differs from its predicates in three ways, related to the primary technological characteristic difference of the NMR LipoProfile Test, which uses nuclear magnetic resonance (NMR) spectroscopy as compared to chemistry-based spectrophotometric detection.

- NMR uses a different energy source – magnetic resonance versus photometric,
- NMR directly measures lipoprotein particles – direct measure of particle number concentration versus chemistry-based lipid assay, and
- NMR does not require chemical or enzymatic reactions to measure lipoprotein concentrations.

Therefore, fundamentally the NMR LipoProfile Test and predicates are intended to measure substantially similar information by way of different methods, by evaluating the quality and quantity of lipoproteins in biological specimens using proprietary algorithms, physical measurements, and calculations. Although the NMR LipoProfile Test differs in technological characteristics, the performance of this assays has been shown to be equivalent through the testing of clinical specimens. For LDL-P, substantial equivalence and clinical utility was demonstrated in the target population utilizing appropriate clinical outcome measures and for the measurement of triglycerides and HDL-C, comparing the NMR test results to standard chemical methods for TRIG and HDL-C determination.

Performance Data - Non-Clinical

Analytical Sensitivity

The analytical sensitivity of the NMR LipoProfile test measurements of LDL-P, HDL-C, and triglycerides was determined as the lowest concentration measurable with acceptable precision and accuracy. Serum specimens with low initial concentrations LDL-P, HDL-C, and triglycerides were serially diluted and 20 replicates of each were analyzed. CVs and % bias between observed and target values were determined and acceptance criteria are based on total error ≤20%. Limits of quantification (LOQ) are 300 nmol/L for LDL-P, 10 mg/dL for HDL-C, and 25 mg/dL for triglycerides.

Assay Precision

Intra-assay and inter-assay variability were determined by testing 20 replicates of two patient serum pools in the same run (intra-assay) and in 20 different runs over 4 days (inter-assay). The results of this testing are summarized below:

	Intra-assay Precision						***Inter-assay Precision***					
	Pool 1			Pool 2			Pool 1			Pool 2		
	Mean	**SD**	**% CV**	**Mean**	**SD**	**% CV**	**Mean**	**SD**	**% CV**	**Mean**	**SD**	**% CV**
LDL-P (nmol/L)	2222	49.1	2.2	1042	47.7	4.6	1925	66.7	3.5	1053	68.4	6.5
HDL-C (mg/dL)	41	0.54	1.3	57	0.42	0.7	42	1.17	2.8	56	0.83	1.5
Trig (mg/dL)	189	2.0	1.1	75	1.2	1.5	219	2.9	1.3	80	1.7	2.1

Linearity

Two serum pools were prepared from patient specimens with high or low values of LDL-P, HDL-C, and triglycerides as determined by NMR LipoProfile analysis. Each were mixed and diluted in different proportions to produce 12 different samples with widely varying target concentrations. Mean values from analysis of 6 replicates were compared to the expected target values to determine the percent bias for each sample. Linear ranges were determined as follows:

LDL-P	300-6000 nmol/L
HDL-C	7-160 mg/dL
Triglycerides	5-2700 mg/dL

Reportable Range

The following are the reportable ranges for LDL-P, HDL-C and triglycerides.

LDL-P	300 – 3500 nmol/L
HDL-C	7 - 140 mg/dL
Triglycerides	5 - 1100 mg/dL

Interfering Substances

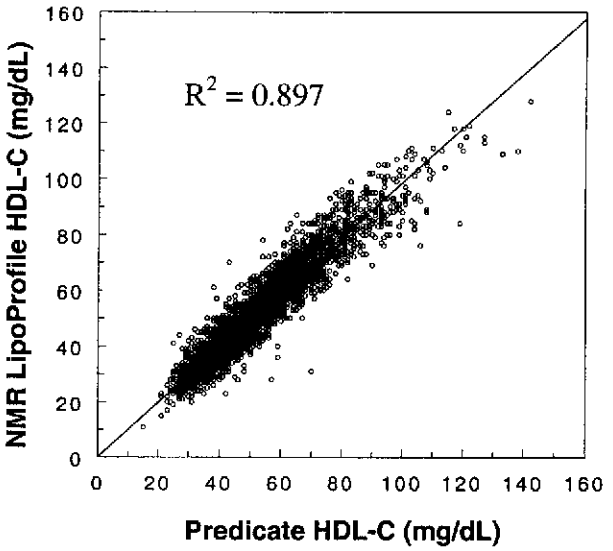
Endogenous substances normally found in blood and exogenous substances (common and prescription drugs) were evaluated for potential interference with the NMR LipoProfile test. Six plasma pools with LDL-P, HDL-C, and triglyceride values spanning the clinically-relevant range were spiked with potential interferents. No appreciable interference was produced by the substances at the spiked levels tested, which were representative of the highest blood concentrations expected for the highest therapeutic doses of these compounds.

Potential Interferent	***Test Concentration***
Endogenous	
Bilirubin	20 mg/dL
Creatinine	20 mg/dL
Hemoglobin	500 mg/dL
Urea	300 mg/dL
Uric acid	40 mg/dL
Exogenous	
Acetaminophen	1050 µmol/L
Aspirin	880 µmol/L
Clopidogrel	28 µmol/L
Enalapril	13 µmol/L
Fenofibrate	70 µmol/L
Furosemide	38 µmol/L
Glipizide	7 µmol/L
Hydralazine	60 µmol/L
Hydrochlorothiazide	27 µmol/L
Ibuprofen	550 µmol/L
Isosorbide dinitrate	80 µmol/L
Metformin	960 µmol/L
Metoprolol	23 µmol/L
Naproxen	470 µmol/L
Niacin	2200 µmol/L
Nifedipine	37 µmol/L
Piroxicam	10 µmol/L
Simvastatin	30 µmol/L
Thiazolidinedione	61 µmol/L
Triamterene	31 µmol/L

Performance Data - Clinical

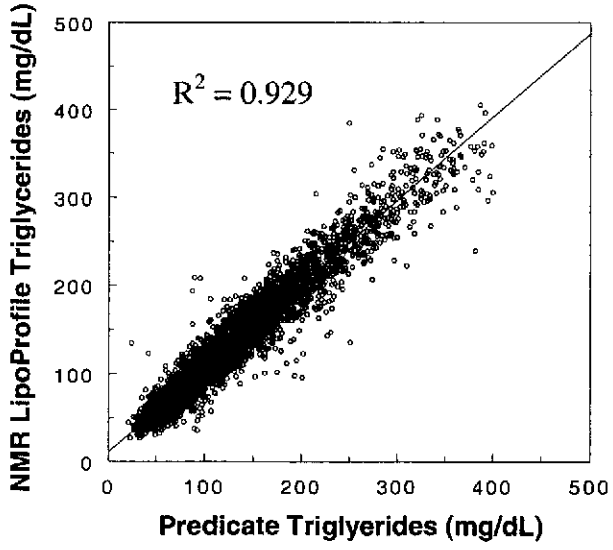
Method Comparison - HDL Cholesterol

Method comparison was evaluated by split-sample comparison of HDL-C values measured by the NMR LipoProfile test with those analyzed on a commercially available chemistry analyzer system. The data below summarize the results of analyses performed on 5,362 plasma samples from individuals who were part of the Multi-Ethnic Study of Atherosclerosis (MESA). HDL-C concentrations ranged from 15 to approximately 140 mg/dL and the mean values observed for the predicate and the NMR LipoProfile test were 51.3 and 50.7 mg/dL, respectively.



Method Comparison - Triglycerides

Method comparison was evaluated by split-sample comparison of triglyceride values measured by the NMR LipoProfile test with those analyzed on a commercially available chemistry analyzer system. The data below summarize the results of analyses performed on 5,362 plasma samples from individuals who were part of the Multi-Ethnic Study of Atherosclerosis (MESA). Triglyceride concentrations ranged from 21 to 400 mg/dL and the mean values observed for the predicate and the NMR LipoProfile test were 123.9 and 128.7 mg/dL, respectively..



Clinical performance of NMR LipoProfile test for LDL-P Measurement

Three external clinical outcome studies were conducted to evaluate the clinical performance of the NMR Lipoprofile measurement of LDL-P. The studies estimated the prediction of future (incident) cardiovascular disease (CVD) events by previously measured values of LDL-P. Results of all three studies indicated that LDL-P was statistically significantly related to CVD risk

Veterans Affairs HDL Intervention Trial (VA-HIT)

A prospective, nested case-control study was conducted using 1061 plasma samples collected from male patients enrolled in the randomized placebo-controlled Veterans Affairs HDL Intervention Trial (VA-HIT), a secondary prevention trial examining the efficacy of gemfibrozil for prevention of new CHD events among men with known CHD and low levels of both HDL and LDL cholesterol. Fasting EDTA plasma samples were collected at baseline and after 7 months from 2,531 men. Case subjects (n=364) were men who experienced a CHD event (cardiac death or nonfatal myocardial infarction) during the mean 5.1 year follow-up period. Control subjects (n=697) were men matched for age who remained free of CHD events during follow-up.

Table 1 shows the odds ratios (OR) for a new CHD event associated with a 1- SD increment of LDL-P in the subjects treated with placebo (n=546). Baseline levels of LDL-P were statistically significantly associated with incident CHD events (odds ratio 1.31 (95% CI, 1.09-1.57, p=0.004), while on-trial LDL-P values had a somewhat weaker association .

Table 1: Prediction of CHD Events by LDL-P in the Placebo Group

	Baseline	***On-Trial***
LDL-P		
Odds Ratio (95% CI)	1.31 (1.09-1.57)	1.19 (0.99-1.43)
p value	0.004	0.054

EPIC -Norfolk study

A nested case-control study was performed in the prospective EPIC (European Prospective Investigation into Cancer and Nutrition)-Norfolk study, which was carried out between 1993 and 1997 to investigate dietary and other determinants of cancer. Additional data were obtained to enable the assessment of determinants of other diseases, including coronary artery disease (CAD). The study population comprised 25,663 men and women inhabitants of Norfolk, United Kingdom, aged 45 to 79 years, who completed a baseline questionnaire survey and attended a clinic visit. At this baseline visit, non-fasting serum samples were obtained from participants and stored at -80°C before NMR LipoProfile testing. Participants were followed for six years for the development of CAD, defined as CAD death, myocardial infarction, and angina. Samples

tested (n=2,888; 36% women; average age 65 years) were from cases (n=1,003) who developed CAD during the 6-year follow-up period and controls (n=1,885) who did not develop CAD, matched for age, gender, and enrollment time. None of the cases or controls were taking any lipid altering medications.

LDL-P values measured in this study spanned the range of 485-4156 nmol/L. Conditional logistic regression was used to calculate odds ratios for future (incident) CAD, adjusted for smoking and blood pressure plus matching for age, gender, and enrollment time. Table 2 shows the odds ratios for development of CAD by increasing quartiles of LDL-P. LDL-P was statistically significantly associated with an incident CAD events in both univariable analyses and multivariable analyses adjusted for HDL-C and triglycerides.

Table 2: Association of Incident Coronary Artery Disease Events by Quartile of LDL-P

	Quartiles				
	1	2	3	4	p[§]
Range (nmol/L)	<1278	1278-1525	1526-1812	>1812	
Univariable Odds Ratio (95% CI)	1.00	1.23 (0.97-1.56)	1.48 (1.17-1.87)	2.00 (1.58-2.59)	<0.0001
Multivariable Odds Ratio (95% CI)	1.00	1.13 (0.89-1.44)	1.21 (0.94-1.54)	1.37 (1.04-1.83)	0.02

Women's Health Study

A study was conducted using 27,673 baseline nonfasting EDTA plasma samples from participants enrolled in the Women's Health Study, a randomized, double blind, placebo-controlled trial of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease (CVD) and cancer in women. Participants were apparently healthy female health care professionals, ages 45 years and older, who were free of self-reported CVD and cancer at study entry and were followed for incident CVD over a mean of 11 years. The CVD endpoint was a composite of nonfatal myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, nonfatal ischemic stroke, and cardiovascular death. 1,015 CVD events occurred during the follow-up period (Mean ± SD = 11 ± 1.6 years; range 0.003 to 12.8 years).

LDL-P values measured in this study spanned the range of 276-4590 nmol/L. Cox proportional hazard regression models were used to examine the association of LDL-P by quintile with incident CVD events. The Cox models were adjusted for age, randomized treatment assignment (to aspirin, vitamin E or placebo), smoking status, menopausal status, postmenopausal hormone use, blood pressure, diabetes, and body mass index. The results, shown in Table 3, indicate that baseline concentrations of LDL-P were statistically significantly associated with incident CVD events ($p<0.001$).

Table 3: Association with Incident Cardiovascular Disease Events by Quintile of LDL-P

	Quintiles					
	1	**2**	**3**	**4**	**5**	**p[§]**
Range (nmol/L)	<963	963-1165	1166-1387	1388-1703	>1703	
HR (95% CI)	1.00	1.37 (1.01-1.85)	1.35 (1.01-1.81)	1.80 (1.36-2.38)	2.51 (1.91-3.30)	<0.001

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL 23 2008

Liposcience Inc.
c/o Mr. E. Duffy McDonald
Vice President Operations, Liposcience
2500 Sumner Blvd.,
Raleigh, NC 27616

Re: k063841
Trade/Device Name: NMR Profiler and NMR LipoProfile® Test
Regulation Number: 21 CFR 862.1475
Regulation Name: Lipoprotein Test System
Regulatory Class: Class I, subject to limitation of exemption in 21 CFR 862.9(c)(4)
Product Code: MRR, JJY, CDT, LBS, JIT
Dated: April 23, 2008
Received: April 24, 2008

Dear Mr. McDonald:

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. 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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0490. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address at http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Jean M. Cooper, M.S., D.V.M.

Jean M. Cooper, M.S., D.V.M.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): k063841

Device Name: NMR Profiler and NMR LipoProfile® Test

Indication 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. The test is performed and provided as a service by Liposcience Laboratory.

Prescription Use ✓ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K063841