NOV 10 1997

510(k) Summary

1. General Information

Date Prepared: January 24, 1997

K970302

Submittor: PerImmune, Inc.
1330 Piccard Drive
Rockville, MD 20850-4396

FDA Establishment Registration Number: 1119752

Contact Person: Peter Manilla, MSc.
Regulatory Affairs Administrator
PerImmune, Inc.
1330 Piccard Drive
Rockville, MD 20850-4396
301-258-5200, extension 1088
301-977-3229 (fax)

2. Device Name

Classification Name: Lipoprotein Immunological Test System

Common or Usual Name: Lipoprotein(a) ELISA

Trade or Proprietary Name: Apo-Tek Lp(a)™

3. Identification of Predicate or Legally Marketed Device(s)

Devices similar to Apo-Tek Lp(a)™ for the determination of lipoproteins have been classified into class II under Section 513(b) of the FD & C Act and under Title 21 of the Federal Code of Regulations, Part 866.5600 (21 CFR 866.5600). Apo-Tek Lp(a)™ is similar in design and function to the Roche Reagent for Apolipoprotein B manufactured by Roche Diagnostics, which was the subject of a Premarket Notification #K910552, and the SPQ™ Test System for Apolipoprotein B manufactured by Atlantic Antibodies, which was the subject of Premarket Notification #K870564

4. Summary

Apo-Tek Lp(a)™ is an apolipoprotein(a) [Apo(a)] isoform independent *in vitro* diagnostic enzyme-linked immunosorbent assay (ELISA) intended for the quantitiative assessment of lipoprotein(a) [Lp(a)] in human serum or plasma. The measurement of Lp(a) in conjunction with other diagnostic tests for atherosclerosis is of diagnostic significance when assessing cardiovascular disease. This test utilizes a sandwich ELISA format in which the Lp(a) particle is captured with a specific anti-Apo(a) monoclonal antibody and, after washing away nonbound serum or plasma components, is detected with a peroxidase conjugated anti-apolipoprotein B [Apo B] polyclonal antibody. This format is designed such that plasma or serum Lp(a) concentrations are accurately quantified regardless of Apo(a) isoform. Apo(a) isoform independence is an important consideration when measuring Lp(a) levels because Apo(a) isoform dependent assays tend to underestimate concentrations of individuals with low molecular weight isoforms who have elevated Lp(a) concentrations. These false negative results lead to potential misclassification of individuals at increased risk of atherosclerotic disease.

A number of clinical methods and *in vitro* diagnostic products for the determination of Apo B containing lipoprotein particles are currently in use to diagnose cardiovascular disease. Apo-Tek Lp(a)™ determines Lp(a) concentrations, a subset of Apo B containing lipoprotein particles, by capturing Lp(a) on a solid phase through its Apo(a) moiety and quantifying its Apo B moiety. Both the Roche Reagent for Apolipoprotein B and the Atlantic Antibodies SPQ™ Test System for Apolipoprotein B determine concentrations of all Apo B containing lipoproteins including Lp(a). Substantial equivalence was shown to these lipoprotein test systems (21 CFR 866.5600) for the measurement of Apo B containing lipoproteins in human serum or plasma. Specifically, Apo-Tek Lp(a)™ has equivalent clinical utility to Roche's Reagent for Apolipoprotein B in identifying individuals with cardiovascular disease. The relationship between Lp(a) measurement and measurement of all Apo B-containing lipoprotein particles was confirmed using the Atlantic Antibodies SPQ™ Test System for Apolipoprotein B.

Apo-Tek Lp(a)™ shows no cross-reactivity with plasminogen up to 1 g/L, a protein structurally similar to Apo(a). This assay also shows no cross-reactivity with the Apo B-containing lipoprotein particles, low density lipoproteins (LDL) up to 10 g/L LDL protein or very low density lipoproteins (VLDL) up to 2 g/L VLDL protein. Triglycerides up to 8.9 g/L, hemoglobin up to 5 g/L, and bilirubin up to 0.05 g/L do not interfere with the test. The minimum Lp(a) level distinguishable from the 0 mg/dL (0 nmol/L) Calibrator is 0.3 mg/dL (0.72 nmol/L). Apo-Tek Lp(a)™ is highly reproducible with total (combined intra- and interassay) coefficient of variation (CV) ranging from 6.4% to 12.8% for samples ranging from 8.8 to 34.8 mg/dL (as determined by NCCLS document EP5-T2). Apo(a) phenotype heterogeneity does not affect assay linearity as indicated by a correlation coefficient (r) of 0.997 or better obtained for five different phenotypes

(spanning the entire range of molecular weights) tested.

Numerous prospective and retrospective studies have shown the strong association of elevated Lp(a) levels with atherosclerosis as manifested by cardiovascular disease (i.e, coronary heart disease and carotid artery disease). Two clinical evaluations of Apo-Tek Lp(a)™ have shown that Lp(a) levels >20 mg/dL independently increased the odds to have had: a myocardial infarction by 2.88-fold, >50% stenosis of at least one coronary artery by 2.88-fold, cerebrovascular disease by 20.3-fold, and carotid artery stenosis (≥20%) by 27.6-fold. These findings were confirmed in a cross-sectional cohort study of a well characterized U.S. population. Specifically, a 1.55-fold increased odds to have had carotid artery disease (≥50% stenosis) and a 1.5-fold increased odds to have had coronary heart disease were observed in the latter study when Lp(a) levels exceeded 20 mg/dL.

These studies also showed that odds ratios increased when Lp(a) measurement was used in conjunction with the measurement of Apo B or LDL cholesterol. Specifically, at elevated Lp(a) and Apo B levels (>20 mg/dL and >178 mg/dL, respectively), the odds of having had a myocardial infarction increased from 2.88 to 3.86 while the odds of having had >50% stenosis of at least one coronary artery increased from 2.88 to 3.52. When both Lp(a) and LDL cholesterol levels were elevated (defined as >20 mg/dL and >130 mg/dL, respectively), the odds of having had ischemic cerebrovascular disease increased from 20.3 to 21.9. These findings were confirmed in a U.S. study, which showed that when both Lp(a) and LDL cholesterol levels were elevated, the odds increased from 1.5 to 1.61 to have had coronary heart disease and from 1.65 to 2.29 to have had carotid artery stenosis (≥50%). Therefore, Lp(a) measurement, in conjunction with measurement of Apo B or LDL cholesterol, is of even greater diagnostic significance when assessing cardiovascular disease (i.e., coronary heart disease or carotid artery stenosis) than any single lipid analyte, thus supporting the indications for the use of this device.

In summary, Lp(a) is an important, independent marker of atherosclerosis, a systemic disease, manifested by cardiovascular disease (which includes coronary heart disease and carotid artery stenosis). Measurement of Lp(a) plasma or serum levels by Apo-Tek Lp(a)™, an Apo(a) isoform independent ELISA, provides the clinician with a valuable aid in assessing atherosclerotic disease and its manifestations when used in conjunction with other diagnostic tests for this disease.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

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Peter Manilla, MSc.
Regulatory Affairs Administrator
PerImmune, Inc.
1330 Piccard Drive
Rockville, MD 20850-4396

Re: K970302
Trade Name: Apo-Tek Lp(a)™
Regulatory Class: II
Product Code: DFC
Dated: July 22, 1997
Received: August 20, 1997

Dear Mr. Manilla:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to 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). 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 (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice requirement, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic (QS) inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal Laws or Regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 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 advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html"

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

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K970302

510(k) Number (if known):

Apo-Tek Lp(a)™

Device Name:

Indications For Use:

Apo-Tek Lp(a)™ is an Apo(a) isoform independent enzyme-linked immunosorbent assay (ELISA) for the quantitative determination of lipoprotein(a) [Lp(a)] in human serum and plasma. The measurement of Lp(a), in conjunction with other lipoprotein tests, is of diagnostic significance when assessing atherosclerotic cardiovascular disease in specific populations.

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K970302

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use ___
(Per 21 CFR 801.109)

(Optional Format 1-2-96)