510(k) Summary

APR - 4 2008

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: K072032

A. Safety and effectiveness information required per [§807.92(a)(1)]:

Submitter's Name/Address	Contact Name/Information
Corgenix, Inc. 11575 Main Street, Suite 400 Broomfield CO 80020	Daniel Simpson Quality Assurance Manager Phone: 303.457.4345 ext. 128 Fax: 303.457.4519 Email: dfsimpson@corgenix.com
Date Summary Revised:	March 31, 2008

B. Safety and effectiveness information required per [§807.92(a)(2)]:

Device Proprietary Name:	IgG Anti-AtherOx™ Test Kit
Common Name:	Anti-Oxidized LDL Complex Antibody ELISA Test
Regulation Name:	Multiple autoantibodies immunological test system
Classification No.:	21 CFR 866.5660
Product Code:	MSV
Review Panel:	Immunology

C. Identification of legally marketed device to which we are claiming equivalence [§807.92(a)(3)]:

a. Proposed Predicate Device Name(s); K Numbers; Manufacturers

REAADS Anti-Cardiolipin IgG/IgM Semi-Quantitative; K022992; Corgenix, Inc.

D. Description of device [§807.92(a)(4)]:

a. Summary and Explanation

The antiphospholipid syndrome (APS) is one of the most common causes of acquired hypercoagulability (thrombophilia) [1,2]. It is frequently diagnosed in the context of a systemic autoimmune disorder such as SLE (secondary APS), however, it may also occur in the absence of an obvious underlying disease (primary APS) [3]. APS is characterized by high titers of antiphospholipid antibodies with thromboembolic events of venous and arterial vasculatures, or with pregnancy morbidity (miscarriages and fetal loss). High titers of

antiphospholipid antibodies in secondary APS increase the risk of thrombosis by at least 2-fold [2]. In both primary and secondary APS, recurrence rates of thrombosis up to 30% and mortality up to 10% in 10 years have been reported [4,5].

Antiphospholipid antibodies are a heterogeneous family of immunoglobulins [6]. Most of these antibodies do not directly recognize phospholipids but instead recognize phospholipid-binding plasma proteins such as β_2GPI and prothrombin. β_2GPI is the most relevant antigenic target for antiphospholipid antibodies clinically associated with thrombosis [7,8]. β_2GPI-dependent anti-cardiolipin (aCL) antibodies may be detected by ELISA tests using immobilized cardiolipin (CL) in the presence of β_2GPI [9,10]. These antibodies also recognize β_2GPI immobilized on oxygenated microtiter plates but not when β_2GPI is immobilized on plain polystyrene plates [11]. These findings suggested that β_2GPI-dependent aCL antibodies recognize an altered conformation of β_2GPI when it is bound to negatively charged phospholipids.

Oxidative stress and oxLDL formation are common in patients with SLE and APS [12] suggesting an important relationship between lipid peroxidation and clotting activation (hypercoagulability). β_2GPI specifically binds to oxLDL [13,14]. OxLDL/β_2GPI complexes have been characterized [15], demonstrated in patients with APS and SLE and implicated as pro-atherothrombotic autoantigens [16]. The physiologic relevance of IgG antibodies to oxLDL/β_2GPI complexes was demonstrated in vitro by the enhanced macrophage uptake of IgG immune complexes containing oxLDL/β_2GPI. The participation of macrophage Fcγ receptors in the uptake of these complexes seems to be particularly important in the development of foam cells, atherosclerotic plaques and arterial thrombosis [13-15]. IgG anti-oxLDL/β_2GPI antibodies in autoimmune patients may further accelerate the development of atherothrombosis [17,18].

Previously, IgG anti-oxLDL/β_2GPI antibodies have been detected in SLE, systemic sclerosis (SSc) and rheumatoid arthritis (RA) patients. SLE and SSc patients had significantly higher anti-oxLDL/β_2GPI antibody levels compared to healthy controls [18-20]. Also, in those studies RA patients had higher antibody levels than the controls but this difference was not statistically significant. IgG anti-oxLDL/β_2GPI antibodies were significantly higher in SLE patient with APS compared to SLE controls without APS. Thus, the presence of circulating IgG anti-oxLDL/$\beta_2$2GPI antibodies seem to be etiologically important and a useful serologic marker for venous and arterial (atherothrombotic) risk in autoimmune patients [21-23].

b. Principle of the Test

This test is an indirect ELISA detecting IgG anti-oxLDL/β_2GPI antibodies. Diluted serum samples, calibrator(s), and controls are incubated in microwells coated with the oxLDL-β_2GPI complex. Incubation allows the IgG anti-oxLDL-

β_2GPI antibody present in the samples to react with the immobilized antigen complex. After the removal of unbound serum proteins by washing, anti-human IgG antibodies, labeled with horseradish peroxidase (HRP), are added forming complexes with the bound IgG anti-oxLDL-β_2GPI antibody. Following another washing step, the bound enzyme-antibody conjugate is assayed by the addition of a solution containing tetramethylbenzidine (TMB) and hydrogen peroxide (H_2O_2) as the chromogenic substrate. Color develops in the wells at an intensity proportional to the serum concentration of IgG anti-oxLDL-β_2GPI antibody.

Results are obtained by reading the OD (optical density or absorbance) of each well in a spectrophotometer. Calibrator sera are provided, with the IgG anti-oxLDL-β_2GPI antibody concentration expressed in G Units. A log-log regression analysis is performed with calibrator values plotted against calibrator mean ODs. Controls and patient results are determined from the calibration curve.

c. Device Description

Plate:	96-well polystyrene microtiter plate, 12 x 8 strips coated with oxLDL/β_2GPI complex (human), blocked and stabilized.
Sample diluent:	PBS/protein-based solution (blue) to dilute patient, reference and controls prior to testing
Calibrators:	Human sera with known values of IgG anti-oxDL/β_2GPI antibodies (units) used to calculate control and patient results
Controls:	Human sera with known normal and positive amounts of IgG anti-oxLDL/β_2GPI antibodies with designated acceptable ranges in G units for quality control of results
Conjugate solution:	PBS/protein-based solution (blue) containing HRP-conjugated goat polyclonal anti-human IgG antibody with stabilizers and preservatives
Substrate:	One-component TMB chromogenic substrate containing tetramethylbenzidine and hydrogen peroxide
Stopping solution:	0.36 N sulfuric acid used to stop color development at the end of the assay
Wash solution:	33X concentrate wash buffer (PBS/Tween 20) (diluted to 1 liter of reagent grade water before use)

E. Intended use of device [§807.92(a)(5)]:

An enzyme-linked immunoassay (ELISA) for the detection of IgG antibodies to complexes formed by oxidized low-density lipoprotein (oxLDL) with β_2-glycoprotein I (β_2GPI) in individuals with systemic lupus erythematosus (SLE) and lupus-like disorders (antiphospholipid syndrome).

F. Technological characteristics [§807.92(a)(6)]:

Table V-1.
Comparison of Technological Characteristics

Technological Characteristic	Corgenix IgG Anti-AtherOx Test Kit	Predicate Device (REAADS IgG Anti-Cardiolipin Test Kit)
INTENDED USE	An enzyme-linked immuno-assay (ELISA) for the detection of IgG antibodies to complexes formed by oxidized low-density lipoprotein (oxLDL) with β_2-glycoprotein I (β_2GPI) in individuals with systemic lupus erythematosus (SLE) and lupus-like disorders (antiphospholipid syndrome).	For the detection and semi-quantitation of anti-cardiolipin antibodies in individuals with systemic lupus erythematosus (SLE) and lupus-like disorders (anti-phospholipid syndrome).
ANALYTE	Detection of IgG anti-phospholipid (anti-oxidized LDL/β_2GPI) antibodies in individuals with autoimmune disease	Detection of IgG anti-phospholipid (anti-cardiolipin) antibodies in individuals with autoimmune disease
Similarities		
ASSAY PRINCIPLE	Indirect ELISA for detection of IgG antibodies to phospholipid antigen	Same for predicate
SPECIMEN TYPE	Serum	Same for predicate (or 3.2% sodium citrate plasma)
LEVEL OF SKILL	High complexity	Same for predicate
TECHNOLOGY	Binding of IgG antibodies in sample to immobilized phospholipid antigen followed by immunological detection	Same for predicate
Differences		
INTERFERING SUBSTANCES	Test not affected by hemoglobin, conjugated bilirubin, lipid or rheumatoid factor	No testing listed in Package Insert

G. Summary of non - clinical testing [§807.92(b)(1)]

a. Analytical Sensitivity

1. Linearity

The linear range of the IgG anti-AtherOx Test Kit was based on protocols specified in CLSI Guideline EP6-A "Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline" with an error goal of ≤ 5 G units between the predicted and recovered values. A strongly-positive sample and a stripped serum pool were mixed at various fixed ratios to produce 11 evenly-spaced concentrations that were predicted to extend past the linear range of the assay. Evaluation of the data indicated that the linear range of the assay was 10 – 100 G units.

2. Precision

The precision of the Corgenix IgG Anti-AtherOx Test Kit was assessed as specified in CLSI EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods. Serum samples with concentrations spanning the range of the assay were tested in the Corgenix laboratory by 2 operators in duplicate on each of 20 days over 30 calendar days. One reagent lot was tested, and assays were calibrated each day.

Sample	Mean Concentration (G Units)	Reproducibility as %CV	Within-Laboratory Precision as %CV
Low	9.6	3%	13%
Med-Low	20.2	4%	12%
Med	28.1	7%	13%
Med-High	38.4	5%	12%
High	76.8	4%	10%

3. Limit of Blank (LOB)/Limit of Detection (LOD)

Limit of Blank and Limit of Detection were assessed according to CLSI Guideline EP17-A *Protocols for Determination of Limits of Quantitation; Approved Guideline*. The Limit of Blank (LoB) was defined nonparametrically at the 95th percentile of the negative results at 6.1 G units. The Limit of Detection (LoD) was defined the lowest level where 5% or fewer of the observed measurements are below the LoB. Since none of the results for the positive data set were at 7.0 G units or below, so the LoD was set as 7 G units.

4. Interfering Substances

The materials in the following list were tested for their potential to interfere in measurements with the Anti-AtherOx Test Kit. The materials were added to five clinical samples with a range of IgG anti-oxLDL-β_2GPI antibody concentrations up to the levels listed.

Hemoglobin	5 mg/mL
Triglycerides	30 mg/mL
Conjugated Bilirubin	0.2 mg/mL
Rheumatoid Factor	500 units/mL

H. Summary of clinical testing [§807.92(b)(2)]:

Serum samples from 205 control patients, 99 patients with rheumatoid arthritis and 143 patients with systemic lupus erythematosus were tested for elevated IgG antiphospholipid antibody levels using the Corgenix IgG anti-AtherOx and REAADS IgG anti-cardiolipin test kits (refer to Table X-3 below). Overall agreement between the two tests was 90.2% (404/448).

The positive/negative results were also compiled within the various disease groups using the cut-offs established for each kit. Refer to Tables V-4, V-5 and V-6 below.

Table V-3.

Assay Results Compilation For Samples From Healthy Controls

Healthy Controls		REAADS IgG Anti-Cardiolipin Pos	REAADS IgG Anti-Cardiolipin Neg
Corgenix IgG Anti-AtherOx	Pos	0	6
	Neg	0	199

Positive Percent Agreement = N/A
Negative Percent Agreement = 97.1% (95% CI = 94.8 – 99.4%)
Overall % Agreement = 97% (95% CI = 94.8 – 99.4%)

Table V-4.
Assay Results Compilation For Samples From Patients With Rheumatoid Arthritis

Rheumatoid Arthritis		REAADS IgG Anti-Cardiolipin	
		Pos	Neg
Corgenix	Pos	1	17
IgG Anti-AtherOx	Neg	0	81

Positive Percent Agreement = 100%
Negative Percent Agreement = 82.7% (95% CI = 75.2 – 90.2%)
Overall % Agreement = 82.8% (95% CI = 75.4 – 90.3%)

Table V-5.
Assay Results Compilation For Samples From Patients With Systemic Lupus Erythematosus

SLE		REAADS IgG Anti-Cardiolipin	
		Pos	Neg
Corgenix	Pos	19	16
IgG Anti-AtherOx	Neg	6	102

Positive Percent Agreement = 76.0% (95% CI = 59.3 – 92.7%)
Negative Percent Agreement = 86.4% (80.3 – 92.6%)
Overall % Agreement = 84.6% (95% CI = 78.7 – 90.5%)

Table V-6.
Assay Results Compilation From Patients With Anti-Phospholipid Syndrome Secondary to SLE

Secondary Anti-Phospholipid Syndrome		REAADS IgG Anti-Cardiolipin	
		Pos	Neg
Corgenix	Pos	17	8
IgG Anti-AtherOx	Neg	6	63

Positive Percent Agreement = 73.9% (95% CI = 56.0 – 91.9%)
Negative Percent Agreement = 88.7% (95% CI = 81.4 – 96.1%)
Overall % Agreement = 85.1% (95% CI = 77.9 – 92.3%)

To compare the performance of the two tests in more defined disease states, the results were separated by APS presentation symptom. These compilations are presented in Table V-7 (A, B, C).

Table V-7 A.
Compilation Of Assay Results Of Patients Who Had Experienced Pregnancy Morbidity

Pregnancy Morbidity		REAADS IgG Anti-Cardiolipin Pos	REAADS IgG Anti-Cardiolipin Neg
Corgenix	Pos	0	1
IgG Anti-AtherOx	Neg	2	12

Positive Percent Agreement = 0%
Negative Percent Agreement = 92.3% (77.8 – 100%)
Overall % Agreement = 80.0% (95% CI = 59.8 – 100%)

Table V-7 B.
Compilation Of Assay Results Of Patients With Arterial Thrombosis

Arterial Thrombosis		REAADS IgG Anti-Cardiolipin Pos	REAADS IgG Anti-Cardiolipin Neg
Corgenix	Pos	11	1
IgG Anti-AtherOx	Neg	3	27

Positive Percent Agreement = 78.6% (95% CI = 57.1 -100%)
Negative Percent Agreement = 96.4% (95% CI = 89.6 – 100%)
Overall % Agreement = 90.5% (95% CI = 84.7 – 100%)

Table V-7 C.
Compilation Of Assay Results Of Patients With Venous Thrombosis

Venous Thrombosis		REAADS IgG Anti-Cardiolipin Pos	REAADS IgG Anti-Cardiolipin Neg
Corgenix	Pos	6	6
IgG Anti-AtherOx	Neg	1	24

Positive Percent Agreement = 85.7% (95% CI = 59.8 – 100%)
Negative Percent Agreement = 80.0% (95% CI = 65.7 – 94.3%)
Overall % Agreement = 81.1% (95% CI = 68.5 – 93.7%)

I. Conclusions from the nonclinical / clinical testing [§807.92(b)(3)]:

The results of the above described studies demonstrate that Corgenix IgG Anti-AtherOx Test Kit is as safe and effective as the cleared predicate device.

J. Additional Information [§807.92(d)]:

No additional information has been requested by the FDA at this time.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

APR - 4 2008

Corgenix, Inc.
c/o Ms. Kimberly Hassler
Director of Quality and Regulatory Affairs
11575 Main St.
Suite 400
Broomfield, CO 80020

Re: k072032
Trade/Device Name: IgG Anti-AtherOx™ Test Kit (IgG antibodies to oxLDL/β2GPI complex)
Regulation Number: 21 CFR 866.5660
Regulation Name: Multiple autoantibodies immunological test system
Regulatory Class: Class II
Product Code: MSV
Dated: March 6, 2008
Received: March 7, 2008

Dear Ms. Hassler:

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 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); 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) 276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. 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 http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Robert L. Becker, Jr., M.D., Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use Statement

510(k) Number: K072032

Device Name: IgG Anti-AtherOx™ Test Kit

IgG-Anti-AtherOx™ Test Kit (IgG antibodies to oxLDL/β2GPI complex)

Indications for Use:

An enzyme-linked immunoassay (ELISA) for the detection of IgG antibodies to complexes formed by oxidized low-density lipoprotein (oxLDL) with β_2-glycoprotein I (β_2GPI) in individuals with systemic lupus erythematosus (SLE) and lupus-like disorders (antiphospholipid syndrome).

Intended User:

The IgG anti-AtherOx™ test kit is intended for use primarily in clinical (hospital and reference) laboratories.

Prescription Use ✓ (Part 21 CFR 801 Subpart D) **AND/OR** **Over-The-Counter Use** ___ (21 CFR 801 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Maria M Chan

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K072032