DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

IMMCO Diagnostics Inc.
Mr. Kevin Lawson
Chief Regulatory Officer
60 Pineview Drive
Buffalo, NY 14228

March 11, 2016

Re: K151559
Trade/Device Name: ImmuLisa™ Enhanced Centromere Antibody ELISA
Regulation Number: 21 CFR §866.5100
Regulation Name: Antinuclear antibody immunological test system
Regulatory Class: Class II
Product Code: LJM, antinuclear antibody (enzyme-labeled), antigen, controls
Dated**: February 5, 2016**
Received**: February 5, 2016**

Dear Mr. Lawson:
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. 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 Parts 801 and 809**]**); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Kelly Oliner -S

For
Leonthena R. Carrington, MBA, MS, MT(ASCP)
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K151559

Device Name
ImmuLisa™ Enhanced Centromere Antibody ELISA

Indications for Use *(Describe)*
An enzyme linked immunoassay (ELISA) for the qualitative or semi-quantitative detection of anti-centromere IgG antibodies in human serum as an aid in diagnosis of limited cutanteous systemic sclerosis / CREST in conjunction with other laboratory and clinical findings.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary

Submitter:	Immco Diagnostics, Inc.
Address:	60 Pineview Dr., Buffalo, NY 14228
Phone Number:	716-691-0091 ext. 110
Contact:	Kevin Lawson
Summary Prepared:	3-6-2016

Device Name:	ImmuLisa™ Enhanced Centromere Antibody ELISA
Common Name:	Centromere Antibody ELISA
Product Code:	LJM, Antinuclear Antibody (Enzyme-Labeled), Antigen, Controls
Substantially Equivalent to:	INOVA QUANTA Lite™ Centromere ELISA

General Description: Antinuclear antibodies (ANA) occur in sera of patients with various connective tissue disorders such as systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), systemic sclerosis / scleroderma (SSc), polymyositis and Sjögren's syndrome. These ANA are directed against nuclear antigens, including DNA, nucleohistone and various extractable nuclear antigens (ENA) such as RNP, Sm, SS-A (Ro), SS-B (La), Centromere, Scl-70 (topoisomerase I) and Jo-1.

The anti-centromere antibody produces a discrete speckled pattern in HEp-2 immunofluorescence assays, and has been observed in 38-64% of patients with the limited cutaneous systemic sclerosis (lcSSc) or CREST syndrome variant of systemic sclerosis or scleroderma. Centromere antibodies bind the kinetochore of mitotic chromosomes and the pre-kinetochore of interphase cells. Immunoblotting analysis indicates that centromere antibodies recognize at least six epitopes on three chromosomal proteins: CENP-A (17-19kD), CENP-B (80kD), and CENP-C (140kD). CENP-A and CENP-B have been cloned and while CENP-B is thought to be the primary autoantigen, it appears that assays incorporating both antigens produce results with greater sensitivity and more comparable to immunofluorescence.

This test is performed as a solid phase immunoassay. Microwells are coated with recombinant purified CENP-A and CENP-B centromere antigens. Controls, calibrators and patient sera are incubated in the antigen coated wells to allow specific antibodies present in the serum to bind to the centromere antigen. Bound antibodies are detected by adding an enzyme labeled anti-human IgG conjugate. Specific enzyme substrate (TMB) is then added and the presence of antibodies is detected by a color change that is read by a spectrophotometer at 450 nm. Results are expressed in ELISA units per milliliter (EU/ml) and reported as positive or negative.

Intended Use: An enzyme linked immunoassay (ELISA) for the qualitative or semi-quantitative detection of anti-centromere IgG antibodies in human serum as an aid in diagnosis of limited cutaneous systemic sclerosis / CREST in conjunction with other laboratory and clinical findings.

Similarities and Differences: Both kits use recombinant CENP-A and CENP-B coated on 96 well plates to detect IgG Centromere antibody with HRP anti-human IgG conjugate and TMB substrate. The IMMCO kit utilizes a 5 point calibrator curve with a borderline/indeterminate range of 20-25EU/ml; while the INOVA kit uses a single low positive sample as a calibrator and has a cutoff of 20 units with no borderline range.

Non-clinical Tests:

Method Comparison: Both kits were tested with well-characterized lcSSc / CREST subjects and disease controls.

		INOVA Centromere Ab ELISA		
		Positive	Negative	Total
IMMCO	Positive	55	16	71
Centromere Ab	Negative	4	332	336
ELISA	Total	59	348	407

Positive Percent Agreement: 93.2% (95% CI 82.7% - 97.8%)
Negative Percent Agreement: 95.4% (95% CI 92.5% - 97.3%)
Overall Agreement: 95.1% (95% CI 92.4% - 96.9%)

Cross Reactivity:

A total of 669 potentially co-incident antibody positive or cross-reactive specimens selected from individuals suffering from other autoimmune or infectious diseases were tested for centromere antibodies using the ImmuLisa™ assay. Indeterminate samples were considered positive.

Condition	n	Centerome Ab Pos
Diffuse cutaneous scleroderma	39	1
Anti-phospholipid syndrome	36	4
Anti-phospholipid syndrome with SLE	20	0
Celiac Disease	35	2
Churg-Strauss syndrome	27	0
Crohn's disease	25	0
Granulomatosis with polyangitis	27	0
Graves' disease	20	0
Hashimoto's thyroiditis	20	0
Osteoarthritis	20	0
Polymyositis/Dermatomyositis	30	1
Rheumatoid Arthritis	24	1
Sjögren's Syndrome	37	2
Systemic Lupus Erythematosus	92	1
Thrombocytopenia	15	2
Ulcerative Colitis	25	0
Cytomegalovirus	20	0
Hepatitis C	20	0
Herpes simplex virus type 1	20	3
Herpes simplex virus type 2	20	0
Lyme disease	20	0
Mononucleosis	20	1
Rubella	20	0
Syphilis	17	0
Toxoplasmosis	20	0
Total	669	18 (2.7%)

Precision

Precision was tested with positive specimens selected throughout the range of the assay. Seven patients were run in duplicate, twice per day for 20 days (n=80 replicates per sample). Assays were run by two operators on two different sets of equipment.

	Mean	Total Imprecision		Between days		Between Operator		Within run (Repeatability)	
S#	EU/ml	SD	CV%	SD	CV%	SD	CV%	SD	CV%
1	8.5	0.5	6.0	0.3	3.3	0.2	2.8	0.3	4.1
2	16.4	1.1	7.0	0.8	5.2	0.6	3.6	0.5	3.0
3	20.4	1.1	5.6	0.5	2.3	0.5	2.5	0.9	4.4
4	23.8	1.1	4.6	0.8	3.5	0.5	2.2	0.5	1.9
5	49.0	3.1	6.2	2.2	4.5	1.5	3.1	1.5	3.0
6	105.1	4.0	3.8	2.7	2.6	2.4	2.3	1.7	1.6
7	150.6	5.3	3.5	2.0	1.4	2.8	1.9	4.0	2.7

Reproducibility

Qualitative reproducibility was tested with 80 runs of samples in the negative range, ~20% below cutoff, ~20% above cutoff, in the moderate positive range of the assay and near the cutoff using the qualitative analysis method. Samples were tested in duplicate twice per day for 20 days be two different operators / equipment sets. Assay results for the cutoff specimen produced 62.5% qualitative (positive) agreement. Assay results for the ~20% above cutoff specimens produced 98.8% qualitative agreement. All other specimens produced 100% qualitative agreement.

Limit of Detection

The limit of detection (LoD) was determined based on 60 replicates of the blank and 10 replicates each of 6 low-level (NHS) samples. LoD was determined to be 3.9 EU/ml.

Linearity and Recovery

Linearity and recovery were tested by diluting positive specimens through the assay range in equidistant dilutions and comparing actual vs. expected results. The linear range of the assay was determined be 3.9 (LoD) – 160 EU/ml. Results are summarized below:

Test Range (EU/ml)	Slope (95% CI)	Y-intercept (95% CI)	R^2	% recovery
3.2 to 46.0	1.05 (0.97 to 1.13)	-0.67 (-2.88 to 1.53)	0.9942	92% to 116%
6.3 to 123.1	1.02 (0.95 to 1.10)	-0.18 (-5.64 to 5.29)	0.9947	93% to 104%
4.9 to 188.1	1.03 (0.95 to 1.11)	1.42 (-7.15 to 9.98)	0.9842	87% to 102%

To assess hook effect, dilutions of high positive specimens with results above the 160 EU/ml measuring range were tested. Hook effect was not demonstrated in dilution samples with theoretical levels of 2531.3 EU/ml for testing within OD range of the microplate reader (~3.5OD).

Clinical Tests: Sets of clinical samples were tested on the IMMCO Centromere ELISA. By testing 124 lcSSc/CREST samples the sensitivity was determined to be 53.2%. By testing 865 autoimmune and infectious disease controls the specificity was determined to be 95.5%.

Kevin J. Lawson
VP Regulatory Affairs

60 Pineview Drive ● Buffalo, NY 14228-2120 ● USA
Toll free (800) 537-8378 ● tel. (716) 691-0091 ● fax (716) 691-0466

www.immco.com