IMMCO Diagnostics, Inc.
Mr. Kevin Lawson
Chief Regulatory Officer
60 Pineview Dr.
Buffalo, New York 14228

March 30, 2018

Re: K172078
Trade/Device Name: ImmuLisa Enhanced RNA POL III Antibody ELISA
Regulation Number: 21 CFR 866.5100
Regulation Name: Antinuclear antibody immunological test system
Regulatory Class: Class II
Product Code: NYO
Dated: July 7, 2017
Received: July 10, 2017

Dear Kevin 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 Part 801 and Part 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.

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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kelly Oliner -S

For
Lea Carrington
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)*
K172078

Device Name
ImmuLisa™ Enhanced RNA POL III Antibody ELISA

Indications for Use *(Describe)*
An enzyme linked immunoassay (ELISA) for the qualitative or semi-quantitative detection of anti-RNA POL III IgG antibodies in human serum as an aid in diagnosis of systemic sclerosis (scleroderma) 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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

ImmuLisa™ Enhanced RNA POL III Antibody ELISA 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: 3-22-2018

Device Name: ImmuLisa Enhanced™ Anti-RNA POL III Antibody ELISA
Common Name: Anti-RNA POL III Antibody ELISA
Product Code: Autoantibodies, anti-ribonucleic acid polymerase (RNAP) III antibody [NYO]
Substantially Equivalent to: INOVA QUANTA Lite™ RNA POL III 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), Jo-1 and RNA polymerase III (RNA POL III). These antigens are macromolecular complexes of protein and RNA.
Systemic sclerosis is associated with many autoantibodies. The anti-centromere antibody has been observed in a large percentage of patients with limited cutaneous systemic sclerosis (lcSSc) or CREST syndrome (Calcinosis, Raynaud's phenomenon, esophageal motility abnormalities, sclerodactylia and telangiectasia) variant of systemic sclerosis or scleroderma. The anti-Scl-70 antibodies are associated with systemic sclerosis with the risk of diffuse skin involvement. The anti-RNA Pol III antibodies are also predictive of diffuse skin involvement, as well as a predictor for the development of hypertensive renal crisis. Anti-RNA Pol III antibodies are frequently found without the presence of anti-Scl-70 or anti-centromere antibodies in patients with systemic sclerosis.
This test is performed as a solid phase immunoassay. Microwells are coated with recombinant RNA POL III antigen. Controls, calibrators and patient sera are incubated in the antigen coated wells to allow specific antibodies present in the serum to bind to the RNA POL III 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-RNA POL III IgG antibodies in human serum as an aid in diagnosis of systemic sclerosis (scleroderma) in conjunction with other laboratory and clinical findings.

Similarities and Differences: Both kits use recombinant RNA POL III coated on 96 well plates to detect IgG RNA POL III 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 20-25 EU/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 systemic sclerosis subjects and disease controls. Semi-quantitative results are presented below. Qualitative results are the same as the borderline considered positive results.

		Other RNA POL III Ab ELISA		
		Positive	Negative	Total
IMMCO RNA POL III Ab ELISA	Positive	41	1	42
	Borderline	9	1	10
	Negative	2	359	361
	Total	52	361	413

Borderline considered positive

Positive Percent Agreement: 96.2% (95% CI 85.7% - 99.3%)
Negative Percent Agreement: 99.4% (95% CI 97.8% - 99.9%)
Overall Agreement: 99.0% (95% CI 97.8% - 99.7%)

Borderline considered negative
Positive Percent Agreement: 78.8% (95% CI 64.9% - 88.4%)
Negative Percent Agreement: 99.7% (95% CI 98.2% - 100.0%)
Overall Agreement: 97.1% (95% CI 95.0% - 98.3%)

Cross Reactivity

Sets of clinical samples were tested to on the ImmuLisa™ RNA POL III ELISA. Populations included systemic sclerosis sera as well as autoimmune and infectious disease controls.

Population	n	n Positive*	% Positive
Systemic sclerosis (SSC)	281	65	23.1%
Diffuse cutaneous SSc (dcSSc)	105	61	58.1%
Limited cutaneous SSc (lcSSc)	176	4	2.3%
Systemic lupus erythematosus	40	0	0.0%
Sjögren's syndrome	41	0	0.0%
Myositis	40	1	2.5%
Rheumatoid arthritis	40	1	2.5%
HSV-1	20	0	0.0%
HSV-2	20	0	0.0%
Lyme	20	0	0.0%
Toxoplasmosis	20	0	0.0%
CMV	20	0	0.0%
Rubella	20	0	0.0%
Syphilis	20	0	0.0%
Hepatitis C	20	1	5.0%
Autoimmune hepatitis	13	0	0.0%
Acute renal failure	29	0	0.0%
Breast Cancer	7	1	14.3%
Colorectal Cancer	10	0	0.0%
Ovarian Cancer	10	0	0.0%
Pancreatic Cancer	10	0	0.0%
Esophageal reflux	31	1	3.2%
Hypertension	27	1	3.7%
MCTD	19	1	5.3%
Morphea	2	0	0.0%
Pulmonary Hypertension	29	0	0.0%
Psoriasis	27	3	11.1%
Raynauds	13	0	0.0%
Vitiligo	1	0	0.0%

Precision

Precision was tested with positive and negative 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 with two different operators / equipment sets.

		Total Imprecision		Within day		Between days		Within run (Repeatability)	
S#	Mean EU/ml	SD	CV%	SD	CV%	SD	CV%	SD	CV%

1	10.0	0.7	7.3%	0.7	7.3%	0.0	0.0%	0.5	5.1%
2	18.2	0.8	4.4%	0.8	4.4%	0.0	0.0%	0.4	2.2%
3	19.6	0.9	4.8%	0.9	4.7%	0.2	1.0%	0.6	2.8%
4	22.0	1.3	5.8%	1.2	5.4%	0.5	2.3%	1.1	4.9%
5	46.2	3.6	7.8%	3.4	7.3%	1.3	2.7%	2.4	5.3%
6	82.8	5.2	6.2%	5.0	6.1%	1.2	1.4%	3.8	4.6%
7	159.0	9.4	5.9%	9.3	5.8%	1.2	0.7%	5.6	3.5%

Reproducibility

Qualitative reproducibility was tested with 40 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 by two different operators / equipment sets. Assay results for the cutoff specimen produced 60% qualitative (positive) agreement. The sample that was ~20% above cutoff produced 98% qualitative (positive) 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 on kits from two different lots. LoD was determined to be 3.2 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 3.2 (LoD) – 160 EU/ml. Results are summarized below:

Test Range (EU/ml)	Slope (95% CI)	Y-intercept (95% CI)	R^2	% recovery
2.5 to 33.5	1.02 (0.96 to 1.10)	-0.15 (-1.72 to 1.43)	0.9943	96% to 117%
8.0 to 66.1	0.98 (0.95 to 1.01)	1.56 (0.13 to 2.98)	0.9987	97% to 109%
31.8 to 169.5	0.99 (0.88 to 1.09)	-2.68 (-14.56 to 9.20)	0.9890	91% to 103%

Interference

Interference was studied by mixing sera with known RNA POL III antibody levels with negative serum samples spiked with potential interferents and studying deviation from expected results. No significant interference was demonstrated for the following substances at the levels indicated: hemoglobin (2 g/L), bilirubin (342 µmol/L), rheumatoid factor (100 EU/ml), cholesterol (13 mmol/L), triglycerides (37 mmol/L), prednisone (0.84 µmol /L), Naproxen (25 mg/ml), Methotrexate (2 mmol/L, Enalapril (0.86 umol/L, Sildenafil (12.9pmol/L), Amlodipine (245 umol/L), Cyclophosphamide (1437 umol/L), Omeprazole (17.4 umol/L), Metoclopramide (1.5 umol/L), Doxycycline (67.5 umol/L), Bosentan (3ug/ml), Tocilizumab (549ug/ml), Mycophenolate mofetil (14.01 ug/ml) and Heparin (3000 U/L).

Clinical Study: Sets of clinical samples were tested on the IMMCO RNA POL III ELISA as described in the Cross Reactivity section. This included 281 systemic sclerosis samples and 549 autoimmune and infectious disease controls.

Systemic sclerosis Clinical Sensitivity: 23.1% (95% C.I. 18.4-28.6%)
Systemic sclerosis Clinical Specificity: 98.2% (95% C.I. 96.6-99.1%)

Indeterminate samples for these studies were considered positive. NHS were excluded in sensitivity/specificity calculations.

Kevin J. Lawson
Chief Regulatory Officer

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

www.immco.com