K131330

GOLD STANDARD DIAGNOSTICS

JAN 28 2014

510(k) Summary

This 510(k) summary of safety and effectiveness information is being submitted in accordance with the requirement of SMDA 1990 and 21 CFR 807.92.

1) **Submitter's Name:** Gold Standard Diagnostics
   Address: 2851 Spafford St. Davis, CA. 95618
   Phone Number: 530-759-8000
   Contact Person: Napoleon Monce
   Date: January 28, 2014

2) **Product and Trade Name:**
   Anti-Nuclear Antibody (ANA) Screen ELISA Test

   Common Name or Classification Name:
   Anti-Nuclear Antibody ELISA

   Product Code:
   LJM

3) **Legally marketed device to which the submitter claims equivalence:**
   Aesku, Inc. Aeskulisa ANA HEp-2 k040953.

4) **Description of the device:**
   The assay requires a total of 90 minutes incubation time. The test uses antigen coated on microtiter wells. Serum is added to each well and incubated for 30 minutes at room temperature. If antibodies are present they will bind to the antigen in the well. Unbound serum is removed by washing the wells three times. An HRP-conjugated anti-human IgG is then added to each well and incubated for 30 minutes at room temperature. If antibody is present, it will bind to the antibody attached to the antigen on the well. The wells are again washed three times to remove any unbound conjugate. A TMB substrate is added to each well and incubated for 30 minutes at room temperature. If enzyme is present, it will react with the substrate to generate a colored product. After the incubation period, the reaction is stopped with a Stop Solution and the color intensity is measured spectrophotometrically.

5) **Intended use of the device:**
   The Gold Standard Diagnostics Antinuclear Antibody (ANA) Screen ELISA Test Kit is a qualitative assay for the detection of ANAs in human serum. The assay collectively detects in one well ANAs against double stranded DNA (dsDNA), SSA (Ro60 and Ro52), SSB (La), Sm, Sm/RNP, Scl-70, Jo-1, Ribosomal P, and Centromeric antibodies along with sera positive for immunofluorescent HEp-2 ANAs.
   The assay is used as an aid in the diagnosis of Systemic Lupus Erythematosus, Mixed Connective Tissue Disease, Sjögren's Syndrome, Progressive Systemic Sclerosis, and

Polymyositis/Dermatomyositis and should be used in conjunction with other laboratory tests and clinical findings.

6) **Comparison with the predicate device:**

The Gold Standard Diagnostics Antinuclear Antibody (ANA) Screen ELISA Test Kit was compared to a commercially available kit manufactured by Aesku Inc, the Aeskulisa ANA HEp-2 (K040953). Below are tables comparing the two devices.

Similarities		
Item	**Device**	**Predicate**
Intended Use	Qualitative assay for the detection of ANAs in human serum.	Same
Assay Format	Qualitative	Same
Technology	ELISA	Same
Calibration	Relative evaluation	Same
Assay Platform	96-well microtiter plates	Same
Controls	Cutoff, Positive and Negative	Same
Conjugate	IgG Conjugate – Anti Human HRP	Same
Substrate	Tetramethylbenzidine (TMB)	Same
Procedure	Sample incubations with micro-well antigen coated plate, followed by a wash step, incubation with an anti-human IgG enzyme conjugate, wash step, incubation with substrate, then addition of a stop solution and reading at 450nm.	Same
Reported Results	OD Ratio	Same
Sample Types	Serum	Same
Sample Dilution	1:101	Same

Differences		
Item	**Device**	**Predicate**
Antigen Mixture	dsDNA, SSA (Ro60 and Ro52), SSB (La), Sm, Sm/RNP, Scl-70, Jo-1, Ribosomal P, and Centromeric antibodies along with sera positive for immunofluorescent HEp-2 ANAs	dsDNA, histones, SSA (Ro), SSB (La), Sm, snRNP/Sm, Scl-70, Jo-1, and Centromeric antibodies along with sera positive for immunofluorescent HEp-2 ANAs
Diluent	Ready to Use	5x concentrate
Wash Solution	10x concentrate	50x concentrate
Stop Solution	1N Sulfuric Acid	1N Hydrochloric Acid
Interpretation	Convert to units. Negative <0.83 units; Equivocal units 0.83-1.2 units; Positive >1.2 units	Convert to Index Value. Negative <1.0 Index Value; Positive >1.0 Index Value

6(b1) Nonclinical tests:

Interfering Substances

The effect of potential interfering substances on samples using the Gold Standard Diagnostics Antinuclear Antibody (ANA) Screen ELISA Test was evaluated. Five samples across the reportable range of the assay were spiked with high levels of hemoglobin, bilirubin, rheumatoid factor, and triglycerides. The recommended concentrations from the guideline "Interference Testing In Clinical Chemistry" from the Clinical and Laboratory Standards Institute were used (CLSI EP7-A2). In addition, to assess the interference in the assay from heterophile antibody, two samples at differing unit values were assessed at three concentrations of a Heterophile (HAMA type 1). The tested substances did not affect the performance of the Gold Standard Diagnostics Anti-Nuclear Antibody (ANA) Screen ELISA Test. The results are summarized below:

Substance	Concentration	Mean Percent Inhibition
Hemoglobin	2 g/L	-2.1%
Bilirubin	20 mg/dL	-3.0%
Rheumatoid Factor	100 IU/mL	8.8%
Triglycerides	3000 mg/dL	-1.4%
Heterophile	65 µg/mL	5.4%
Heterophile	32.5 µg/mL	2.2%
Heterophile	16.25 µg/mL	-0.6%

Prozone (Hook) Effect

To evaluate the hook effect on the Gold Standard Diagnostics Anti-Nuclear Antibody (ANA) Screen ELISA Test, sera with high antibody concentration were tested. Five samples with high antibody titers were diluted 1:100 to 1:12,000 and the ratio of the sample OD to cutoff OD was calculated. The maximum ratio calculated without observing a prozone effect was 12.

6(b2): Clinical Comparison:

The performance of the Gold Standard Diagnostics Anti-Nuclear Antibody (ANA) Screen ELISA assay was determined by conducting a correlation study tested at three different sites using a total of 848 samples. The samples were tested on both the Gold Standard Anti-Nuclear Antibody (ANA) Screen ELISA assay and a commercially available Anti-Nuclear Antibody ELISA test. The results are summarized in the following table:

Overall Results		Predicate Device		
		Positive	Negative	**Total**
Gold Standard Diagnostics ANA Screen ELISA	Positive	251	22	**273**
	Equivocal	7	23	**30**
	Negative	14	531	**545**
	Total	**272**	**576**	**848**

When the equivocal results are treated as positives, the percent positive agreement, percent negative agreement, and the overall agreement along with their 95% confidence intervals are found to be

94.9% % (C.I. 91.5%% - 97.2%), 92.2 % (C.I. 89.7% - 94.2%), and 93.0 % (C.I. 91.1% - 95.7%), respectively.

When the equivocal results are treated as negatives, the percent positive agreement, percent negative agreement, and the overall agreement along with their 95% confidence intervals are found to be 92.3% % (C.I. 88.4%% - 95.2%), 96.2 % (C.I. 94.3% - 97.6%), and 94.9 % (C.I. 93.2% - 96.3%), respectively.

To demonstrate the test has a performance comparable to that of the individual analyte assays, five samples known to be positive for each analyte (dsDNA, SS-A/Ro 60, SS-A/Ro 52, SS-B, Sm, Sm/RNP, Scl-70, Jo-1, Ribosomal P, Centromere, and HEp-2 IFA, total of 55 samples) were tested on the proposed ANA Screening test, on an FDA-cleared test that measures each analyte individually, and by ANA HEp-2 IFA test. The percentage of the five samples from each analyte that were positive is shown in the following table:

Sample reactivity	GSD test	Individual analyte assay- % positive										
		DNA	SSA (Ro60)	SSA (Ro52)	SSB	Sm	Sm/RNP	Scl-70	Jo-1	Ribosomal P	Centromere	Hep-2
dsDNA	**100%**	**100%**	60%	20%	20%	40%	40%	0%	0%	20%	0%	100%
SSA (Ro60)	**100%**	60%	**100%**	40%	20%	0%	0%	0%	0%	20%	0%	100%
SSA (Ro52)	**80%** (1 equivocal)	20%	80%	**100%**	20%	0%	0%	0%	0%	0%	0%	80%
SSB	**100%**	20% (1 equivocal)	100%	60%	**100%**	0%	0%	0%	0%	0%	0%	100%
Sm	**100%**	60%	0%	0%	0%	**100%**	100%	0%	0%	0%	0%	100%
Sm/RNP	**100%**	80%	20%	0%	0%	60%	**100%**	0%	0%	40%	0%	100%
SCL-70	**100%**	20%	0%	0%	0%	0%	0%	**100%**	0%	0%	0%	100%
Jo-1	**100%**	0%	20%	40%	0% (1 equivocal)	0%	0%	0%	**100%**	0%	0%	20%
Ribosomal P	**100%**	80%	40%	0%	0%	0%	40%	0%	0%	**100%**	0%	80%
Centromere	**100%**	0%	0%	0%	0%	0%	0%	0%	0%	0%	**100%**	100%
Hep-2	**100%**	40%	40%	0%	20%	20%	40%	20%	0%	40%	0%	**100%**

Analytical Specificity

Ten reference ANA sera from the Centers for Disease Control (CDC) and 10 sera from the Association of Medical Laboratory Immunologist (AMLI) were tested on the Gold Standard Diagnostics Anti-Nuclear Antibody (ANA) Screen ELISA in duplicate. Below are the observed results for each replicate test. All CDC and AMLI samples gave their expected results.

Sample	Specificity	Result 1	Result 2
CDC #1	DNA	Positive	Positive
CDC #2	SS-A/SS-B	Positive	Positive
CDC #3	RNP, SS-A, SS-B	Positive	Positive
CDC #4	RNP	Positive	Positive
CDC #5	Sm	Positive	Positive
CDC #7	SS-A/Ro	Positive	Positive

CDC #8	CENP-B	Positive	Positive
CDC #9	Scl-70	Positive	Positive
CDC #10	Jo-1	Positive	Positive
CDC #12	Ribosomal-P	Positive	Positive
AMLI #1	Negative	Negative	Negative
AMLI #2	SS-A/SS-B	Positive	Positive
AMLI #3	SmRNP	Positive	Positive
AMLI #4	SS-A/Ro	Positive	Positive
AMLI #5	SS-A/SS-B	Positive	Positive
AMLI #6	Scl-70	Positive	Positive
AMLI #7	Jo-1	Positive	Positive
AMLI #8	CENP-B	Positive	Positive
AMLI #9	dsDNA	Positive	Positive
AMLI #10	Negative	Negative	Negative

Clinical Sensitivity and Specificity

Clinically diagnosed connective tissue and non-connective tissue disease sera were evaluated on both the proposed device and on the predicate device. The results are summarized in the following tables:

Clinical Diagnosis	Number Tested	Positive (%)	Equivocal (%)	Negative (%)
Systemic Lupus Erythematosus (SLE)	322	269 (82.9)	11 (3.4)	42 (13)
Systemic Sclerosis (SSc)	40	29 (72.5)	1 (2.5)	10 (25)
Polymyositis (PM)	12	4 (33.3)	2 (16.7)	6 (50)
Dermatomyositis (DM)	15	4 (26.7)	2 (13.3)	9 (60)
PM or DM Overlap	5	1 (20)	1 (20)	3 (60)
Myositis	10	4 (40)	1 (10)	5 (50)
Mixed Connective Tissue Disease (MCTD)	28	28 (100)	0	0
Undifferentiated CTD (UTCD)	3	3 (100)	0	0
Sjögren's Syndrome (SjS)	75	63 (84)	4 (5.3)	8 (10.7)
Total (CTD)	**510**	**405 (79.4)**	**22 (4.3)**	**83 (16.3)**

Clinical Diagnosis	Number Tested	Positive (%)	Equivocal (%)	Negative (%)
Rheumatoid Arthritis (RA)	100	2 (2)	0	98 (98)
Osteoarthritis	20	5 (25)	0	15 (75)
Primary Biliary Cirrhosis (PBC)	8	1 (12.5)	0	7 (87.5)
Autoimmune Hepatitis (AIH)	2	0	0	2 (100)
Hashimoto's Thyroiditis	17	0	0	17 (100)

Grave's Disease	17	0	0	17 (100)
Ulcerative Colitis	5	0	0	5 (100)
Celiac Disease	5	0	0	5 (100)
Primary Anti-phospholipid Syndrome (PAPS)	22	0	0	22 (100)
Granulomatosis with polyangitis (Wegener's)	5	0	0	5 (100)
Total (non-CTD)	**201**	**8 (4)**	**0**	**193 (96)**

Clinical Diagnosis	**Number Tested**	**Positive (%)**	**Equivocal (%)**	**Negative (%)**
Herpes Simplex Virus (HSV)	7	0	0	7 (100)
Epstein Barr Virus (EBV)	7	0	0	7 (100)
Syphilis	7	0	0	7 (100)
Varicella Zoster Virus (VZV)	7	0	0	7 (100)
Mumps	7	0	0	7 (100)
Rheumatoid Factor	7	0	0	7 (100)
Total (other)	**42**	**0**	**0**	**42 (100)**

The clinical sensitivity and specificity compared to the predicate device is summarized in the following tables:

Overall Results		**CTD**	**Non-CTD & others**	
		Positive	Negative	**Total**
Gold Standard Diagnostics ANA Screen ELISA	Positive	404	8	**412**
	Equivocal	22	0	**22**
	Negative	84	235	**319**
	Total	**510**	**243**	**753**

Equivocals considered as Positive: Sensitivity = 83.5% (95% C.I. = 79.1% - 86.0%)
Specificity = 96.7% (95% C.I. = 93.6% - 98.6%)
Overall = 87.8% (95% C.I. = 85.2% - 90.0%)

Equivocals considered as Negative: Sensitivity = 79.2% (95% C.I. = 75.4% - 82.7%)
Specificity = 96.7% (95% C.I. = 93.6% - 98.6%)
Overall = 84.9% (95% C.I. = 82.1% - 87.4%)

Precision

Assessment of the repeatability of the assay was performed on seven samples; three positive samples, one equivocal sample, and three negative samples. One positive sample was diluted with normal human serum to produce a concentration 20% above the positive ratio cutoff (approximately 1.4 U). One negative sample was diluted to 20% below the negative cutoff ratio (approximately 0.70 units). Each sample was tested twice a day for ten days. All the observed results matched the expected results. The results are summarized in the following table:

Sample	Mean (U)	Range (U)	Expected qualitative result	% Observed matching expected result
1	5.60	5.18–5.82	Positive	100%
2	2.56	2.13–2.96	Positive	100%
3	1.36	1.24–1.67	Positive	100%
4	1.06	0.93–1.30	Equivocal	90%
5	0.73	0.62–0.90	Negative	90%
6	0.34	0.27–0.38	Negative	100%
7	0.16	0.12–0.20	Negative	100%

Reproducibility

The reproducibility of the assay was done by testing three samples in duplicate for five days, twice a day, at three sites with two technicians per site. The mean results are summarized in the table below:

Sample	Mean (U)	Site	Range (U)	Expected qualitative result	% Observed result matching expected result
1	0.20	1	0.18-0.24	Negative	100%
1		2	0.18-0.26	Negative	100%
1		3	0.20-0.27	Negative	100%
2	1.45	1	1.05-1.57	Equivocal	95%
2		2	1.06-1.45	Equivocal	95%
2		3	1.4-1.55	Equivocal	100%
3	3.08	1	2.94-3.14	Positive	100%
3		2	2.51-3.18	Positive	100%
3		3	3.04-3.37	Positive	100%

In addition, a lot to lot comparison was performed using three samples, one positive, one equivocal, and one negative sample tested five times each on three different lots. The results are summarized in the table below:

Sample	Mean (U)	Lot Number	Range (U)	Expected qualitative result	% Observed result matching expected result
1	1.474	1	1.42-1.51	Positive	100%
1		2	1.48-1.60	Positive	100%
1		3	1.39-1.47	Positive	100%
2	0.960	1	0.92-0.96	Equivocal	100%
2		2	0.92-1.01	Equivocal	100%
2		3	0.96-1.00	Equivocal	100%

3	0.519	1	0.51-0.58	Negative	100%
3		2	0.50-0.52	Negative	100%
3		3	0.50-0.51	Negative	100%

Expected Values

The expected value for a normal patient is a negative result. However, positive ANA results may be found in apparently healthy individuals. In a study, 12.4% of sera from normal healthy donors gave detectable ANA results (1). To evaluate the expected values, serum from 99 normal blood donors were tested. The mean unit value, standard deviation, and the unit value of the 95th percentile are summarized in the following table:

	Number Tested	**Mean Units**	**SD**	**95th Percentile**
Normal Healthy Males	51	0.62	0.24	1.09
Normal Healthy Females	48	0.55	0.13	0.82

(1) Jaskowski TD. Schroder C. et. al. Screening for Antinuclear Antibodies by Enzyme Immunoassay. Am J Clin Path. 105(4): 468-473. 1996.

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

January 28, 2014

GOLD STANDARD DIAGNOSTICS
C/O MR. NAPOLEON MONCE
DIRECTOR, PRODUCT DEVELOPEMNT
2851 SPAFFORD ST.
DAVIS CA 95618

Re: k131330
Trade/Device Name: Gold Standard Diagnostics Anti-nuclear Antibody (ANA) Screen Elisa Test Kit
Regulation Number: 21 CFR 866.5100
Regulation Name: Antinuclear antibody immunological test system
Regulatory Class: II
Product Code: LJM
Dated: December 19, 2013
Received: December 23, 2013

Dear Mr. Monce:

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 regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance 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 Small Manufacturers, International and Consumer Assistance 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,

Maria M. Chan -S

Maria M. Chan, Ph.D.
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 on last page.

510(k) Number *(if known)*
k131330

Device Name
Gold Standard Diagnostics Antinuclear Antibody (ANA) Screen ELISA Test Kit

Indications for Use *(Describe)*
The Gold Standard Diagnostics Antinuclear Antibody (ANA) Screen ELISA Test Kit is a qualitative assay for the detection of ANAs in human serum. The assay collectively detects in one well ANAs against double stranded DNA (dsDNA), SSA (Ro60 and Ro52), SSB (La), Sm, Sm/RNP, Scl-70, Jo-1, Ribosomal P, and Centromeric antibodies along with sera positive for immunofluorescent HEp-2 ANAs.
The assay is used as an aid in the diagnosis of Systemic Lupus Erythematosus, Mixed Connective Tissue Disease, Sjögren's Syndrome, Progressive Systemic Sclerosis, and Polymyositis/Dermatomyositis, and should be used in conjunction with other laboratory tests 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)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Elizabeth A. Stafford -S