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510(k) Summary of Safety and Effectiveness for the

ADVIA® Centaur Syphilis Assay

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.

A. 510(k) Number: k112343

B. Date of Preparation: November 1, 2011

C. Proprietary and Established Names:

ADVIA® Centaur Syphilis Assay
ADVIA® Centaur Syphilis Quality Control Materials

D. Applicant:

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E. Regulatory Information:

ADVIA® Centaur Syphilis Assay (reagents and calibrators)

1. Regulation section: 21 CFR § 866.3830 Treponema pallidum treponemal test reagents
2. Classification: Class II
3. Product Code: LIP, enzyme linked immunoabsorption assay, treponema pallidum
4. Panel: Microbiology

ADVIA® Centaur Syphilis Quality Control Materials

1. Regulation section: 21 CFR § 862.1660
   Quality control material (assayed and unassayed).
2. Classification: Class I
3. Product Code: MJY; Kit, serological, negative control
   MJX; Kit, serological, positive control
4. Panel: Microbiology

F. Predicate Device:

ADVIA® Centaur Syphilis Assay (reagents and calibrators) and ADVIA® Centaur Syphilis Quality Control Materials are substantially equivalent to the IMMULITE 2000 Syphilis Screen Test System cleared under k091361

G. Device Description:

The ADVIA Centaur syphilis assay is a fully automated, antigen sandwich assay, using direct chemiluminometric technology. The ancillary pack reagent containing acridinium-ester-labeled *T. pallidum* recombinant antigens is added to the sample.

These *T. pallidum* antigens complex with the antibodies in the sample. The solid phase containing biotinylated T. *pallidum* recombinant antigens preformed to streptavidin-coated magnetic latex particles, is then added to the sample. These particles capture the *T. pallidum* antigen-antibody complexes. Antibody-antigen complexes will form if Syphilis antibodies are present in the sample. A direct relationship exists between the level of antibodies to *T. pallidum* present in the patient sample and the amount of relative light units (RLUs) detected by the system. A result of reactive, nonreactive, or equivocal is determined according to the Index Value established with the calibrators.

The Syphilis kit contains the following:

- 1 ReadyPack® primary reagent pack containing ADVIA Centaur Syphilis Solid Phase Reagent (20 mL);

- 1 Ancillary pack containing ADVIA Centaur Syphilis Ancillary Reagent (10mL)

- ADVIA Centaur Syphilis Master Curve card

- 2 vials of Syphilis Low Calibrator (2 mL fill volume)

- 2 vials of Syphilis High Calibrator (2 mL fill volume)

- ADVIA Centaur Syphilis Calibrator Assigned Value cards

In addition Syphilis quality control materials (2 vials of negative control and 2 vials of positive control with 7 mL fill volume each) are provided separately.

H. Intended Use:

The ADVIA Centaur Syphilis (SYPH) assay is an *in-vitro* diagnostics immunoassay for the qualitative determination of antibodies to *Treponema pallidum* in human serum or plasma (EDTA, lithium or sodium heparinized, citrate) using the ADVIA Centaur® and ADVIA Centaur® XP systems as an aid in the diagnosis of syphilis. The ADVIA Centaur Syphilis assay is not intended for blood and tissue donor screening.

ADVIA® Centaur Syphilis Quality Control Materials are for in-vitro diagnostics use to monitor the performance of the Syphilis assay on the ADVIA Centaur® systems. The performance of the SYPH quality control material has not been established with any other Syphilis assay.

I. Substantial Equivalence Information:

Both the predicate device and ADVIA Centaur Syphilis assay employ prepackaged reagents, calibrators and controls for use on automated test systems. A comparison of the important similarities and differences of these assays is provided in the following table:

Item	**New Device:**	**Predicate Device:**
Analyte	antibodies to *Treponema pallidum*	Same
Intended Use	For *in vitro* diagnostic use in the	Same

	qualitative determination of antibodies to *Treponema pallidum*	
Measurement	qualitative	Same
Assay type	direct sandwich immunoassay based on chemiluminescent technology	Enzyme labeled, one-step chemiluminescent immunoassay
Sample type	Serum , Heparinized Plasma, EDTA plasma, citrate plasma	Serum , Heparinized Plasma
Instrument to be used	ADVIA Centaur	IMMULITE 2000
Capture/Detection Antigen/Antibody	Reagent: recombinant antigens TpN17 and TpN15 as biotin conjugates Ancillary pack: recombinant antigens TpN17 and TpN15 as acridinium ester conjugates	Beads coated with purified recombinant antigen TpN17 are linked to enzyme conjugated purified recombinant TpN17 antigen in the reagent.
Cut-Offs	< 0.9 Non-reactive ≥ 0.9 to < 1.1 Equivocal ≥ 1.1 Reactive	< 0.9 Non-reactive ≥ 0.9 to < 1.1 Indeterminate ≥ 1.1 Reactive
Sample Volume	100 µL	100 µL
Interference	Not affected by hemolysis, icterus or lipemia at test levels	Not affected by hemolysis, icterus or lipemia at test levels
Hook Effect	None observed	None observed
Use of Calibrators	Yes	Yes
Calibrators matrix	Human plasma	Human serum
Number of calibrators	two	one
Calibrator fill volume	Liquid, 2 mL	Lyophilized, 4 mL
Use of controls	Yes	Yes
Number of controls	two	two
Control matrix	Human plasma	Human serum
Control fill volume	Liquid, 7 mL	Lyophilized, 6 mL

J. Performance Characteristics

Substantial equivalence was demonstrated by testing several performance characteristics including imprecision, reproducibility, interfering and cross-reactive substances.

a.Precision

Precision estimates were computed according to CLSI document EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline. Within run and total imprecision were evaluated by testing 5 serum based samples (serum sample pools), 3 plasma based samples (2 controls. low and high. and one additional plasma pool) and 2 calibrators (low and high). The elevated levels were spiked with syphilis antigen to achieve appropriate concentrations. The samples were assayed in duplicate over the course of 20 days, two runs per day, for a total of 40 runs and 80 replicates.

Pool	# Repl.	Mean (Index)	Within Run		Between Run		Between Day		Total	
			SD	CV	SD	CV	SD	CV	SD	CV
Calibrator High (plasma) (high positive)	80	8.16	0.14	1.67	0.06	0.78	0.26	3.20	0.30	3.69
Calibrator Low (plasma) (high negative)	80	0.68	0.01	1.81	0.01	0.83	0.02	2.65	0.02	3.32
Control Negative (plasma) (low negative)	80	0.11	0.00	NA	0.00	NA	0.00	NA	0.01	NA
Control Positive (plasma) (moderate pos.)	80	3.84	0.06	1.50	0.04	0.99	0.12	3.22	0.14	3.69
Plasma sample (moderate positive)	80	1.99	0.03	1.44	0.02	1.05	0.06	2.93	0.07	3.43
Serum sample 1 (low negative)	80	0.19	0.00	NA	0.00	NA	0.00	NA	0.01	NA
Serum sample 2 (high negative)	80	0.80	0.01	1.16	0.01	0.86	0.02	2.86	0.03	3.20
Serum sample 3 (low positive)	80	1.28	0.02	1.31	0.01	0.93	0.04	2.79	0.04	3.22
Serum sample 4 (high positive)	80	6.96	0.10	1.45	0.07	0.95	0.25	3.63	0.28	4.02
Serum sample 5 (high positive)	80	21.45	0.41	1.93	0.28	1.29	0.75	3.50	0.90	4.20

b.Reproducibility

The reproducibility study was conducted using two different reagent lots at three external sites. The protocol was run over 10 days, 2 runs per day, and 4 replicates per run for the sample pools, and 8 replicates per run for the negative and positive control materials. Reproducibility data pooled across 3 Sites, data is presented separately for a representative reagent lot.

Pool	# Repl.	Mean	Within Run		Between Run		Between Day		Total	
			SD	CV	SD	CV	SD	CV	SD	CV
Negative Control (plasma) (low negative)	480	0.11	0.004	NA	0.002	NA	0.01	NA	0.01	NA
Serum Pool 1 (low negative)	240	0.18	0.006	NA	0.002	NA	0.01	NA	0.01	NA
Serum Pool 2 (high negative)	240	0.75	0.01	1.3	0.01	1.4	0.01	1.3	0.02	2.3
Serum Pool 3 (low positive)	240	1.20	0.02	1.5	0.02	1.4	0.01	1.2	0.03	2.4
Serum Pool 4 (high positive)	240	6.67	0.10	1.5	0.11	1.6	0.08	1.2	0.17	2.5
Serum Pool 5 (high positive)	240	20.42	0.29	1.4	0.31	1.5	0.31	1.5	0.53	2.6
Positive Control (plasma) (moderate positive)	480	3.56	0.06	1.6	0.04	1.2	0.05	1.4	0.09	2.5

c.Interference

Interference by endogenous substances in the ADVIA Centaur Syphilis assay was evaluated at three syphilis levels (negative, low positive and high positive) using a significance criterion of >10% variance from the control. Each serum pool was spiked with an interferent to the levels indicated in the table below.

Interferent	Tested concentration (up to)
Hemoglobin	500 mg/dL
Conjugated Bilirubin	40 mg/dL
Unconjugated Bilirubin	40 mg/dL
Intralipid	1000 mg/dL

Cholesterol, Total	400 mg/dL
Gamma Globulin	60 mg/dL
Protein, Total (HSA)	11 g/dL
Biotin	500 ng/mL

There was no indication of interference up to the levels claimed.
For the Syphilis positive samples all results demonstrated ≤ 10% change in index value, with the exception of gamma globulin at concentrations above 30 mg/dL..

d.Cross-reactivity

A total of 211 cord blood samples, samples from pregnant women (1st , 2nd, and 3rd trimester), samples from hospitalized patients, pediatric samples and transplant samples were tested using the ADVIA Centaur Syphilis assay and the predicate device (predicate device). Each sample was tested in singlicate using one lot of reagent on one system. Predicate device and Centaur Syphilis results were determined reactive, non-reactive or indeterminate/equivocal according to the respective result interpretation.

		Number of Reactive results	
Clinical Category	**Total Number Tested**	**Centaur Syphilis**	**Predicate device**
Cord Blood	18	1*	1
1st Trimester	24	1*	1
2nd Trimester	25	0	0
3rd Trimester	25	1*	1
Pediatric	48	0	0
Hospitalized	51	2*	2
Transplant Patients			
Heart	1	0	0
Kidney	4	0	0
Liver	6	0	0
Lung	9	0	0

* - positive on predicate device as well

265 specimens from 20 groups of potential cross-reactant disease states were assayed using the ADVIA Centaur Syphilis assay and the predicate device. These samples had a known activity to the potential cross reactant in each group of specimens which was determined by FDA-cleared methods and provided by the respective vendor. Each sample was tested in singlicate using one lot of reagent. The predicate device and Centaur Syphilis results were determined reactive, non-reactive or indeterminate/equivocal according to the respective result interpretation method.

		Number of Reactive results	
Clinical Category	**Total Number Tested**	**Centaur Syphilis**	**Predicate device**
Lyme Disease	10	1*	1
Anti-Nuclear Antibody (ANA)	10	0	0
Rheumatoid Factor	10	0	0
HAMA	10	2*	2

Hepatitis A Infection (HAV) total	20	10*	10
Hepatitis A Infection (HAV) IgM	5	0	0
Hepatitis B Infection (HBV)	10	0	0
Hepatitis C Infection (HCV)	10	0	0
Human Immunodeficiency Virus (HIV)	11	0	0
Cytomegalovirus (CMV) IgG	10	0	0
Cytomegalovirus (CMV) IgM	5	0	0
Epstein-Barr Virus (EBV) IgG	10	0	0
Herpes Simplex Virus (HSV) IgG	10	5*	5
Rubella IgG	10	0	0
Rubella IgM	10	0	0
Toxoplasma IgG	10	1*	1
Toxoplasma IgM	10	0	0
Varicella Zoster Virus (VZV) IgG	10	2*	2
Lupus (SLE)	10	0	0
Drug users	20	3*	3
Myeloma patients	13	0	1
Flu Vaccine recipients	26	0	0
Hyper-IgG	5	0	0
Hyper-IgM	10	0	0

* - positive on predicate device as well.

* - all samples that demonstrated a positive result (with the exception of two HAV-positive samples) were also confirmed positive by other tests (TPPA or RRP), indicating reactivity to Syphilis *(T. Pallidum* antibodies) rather than cross reactivity.

K. Clinical evaluation

As part of the clinical study, samples from various patient populations were tested at three clinical trial sites with both the ADVIA Centaur Syphilis assay and the predicate device. Results are summarized in the following tables.

Method Comparison, All Sites pooled

	Predicate Device			
ADVIA Centaur System	Reactive	Indeterminate	Nonreactive	Total
Reactive	700	1	6	707
Equivocal	1	0	3	4
Nonreactive	14	1	1382	1397
Total	715	2	1391	2108

The negative percent agreement was 99.4% (1382/1391) with a 95% confidence interval (CI) of 98.8 to 99.7%.

The positive percent agreement was 97.9% (700/715) with a 95% confidence interval (CI) of 96.6 to 98.8%.

Method Comparison, Expected Positive Population

Expected Positive Subjects	Reactive	Equivocal	Nonreactive	Total	Positive Percent Agreement
TPPA-Reactive	271 (98.2%)	1 (0.4%)	4 (1.4%)	276	99.6% (271/272)
Medically Diagnosed	264 (92.6%)	0 (0.0%)	21 (7.4%)	285	99.2% (264/266)
Total	535 (95.4%)	1 (0.2%)	25 (4.5%)	561	99.4% (535/538)

The % positive agreement was 99.4% (535/538) with a 95% confidence interval with a 95% confidence interval (CI) of 98.4 to 99.9%, and the % negative agreement was 100% (23/23) with a 95% confidence interval (CI) of 85.2 to 100.0%.

Method Comparison, Samples Sent for Syphilis Testing

	Predicate device			
ADVIA Centaur System	Reactive	Indeterminate	Nonreactive	Total
Reactive	160	1	6	167
Equivocal	0	0	3	3
Nonreactive	3	0	568	571
Total	163	1	577	741

The % positive agreement was 98.2% (160/163) with a 95% confidence interval (CI) of 94.7 to 99.6%, and the % negative agreement was 98.4% (568/577) with a 95% confidence interval (CI) of 97.1 to 99.3%.

Conclusion:
Comparative testing of the ADVIA Centaur Syphilis assay is substantially equivalent in principle and performance to the predicate device.

Kira Gordon
Regulatory Affairs & Compliance
November 1, 2011

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

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JAN 20 2012

Re: K112343
Trade/Device Name: ADVIA Centaur Syphilis Assay
Regulation Number: 21 CFR § 866.3830
Regulation Name: *Treponema pallidum* treponemal test reagents
Regulatory Class: Class II
Product Code: LIP
Dated: January 17, 2012
Received: January 18, 2012

Dear Dr. Gordon:

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 class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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); and 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 advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. 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.

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/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications For Use

510(k) Number: k112343

Device Name:

ADVIA® Centaur Syphilis assay

ADVIA® Centaur Syphilis Quality Control Materials

Indications For Use:

The ADVIA Centaur Syphilis assay:

The ADVIA Centaur Syphilis (SYPH) assay is an *in-vitro* diagnostic immunoassay for the qualitative determination of antibodies to *Treponema pallidum* in human serum or plasma (EDTA, lithium or sodium heparinized, citrate) using the ADVIA Centaur® and ADVIA Centaur® XP systems as an aid in the diagnosis of syphilis.

The ADVIA Centaur Syphilis assay is not intended for blood and tissue donor screening.

ADVIA Centaur Syphilis Quality Control Materials:

ADVIA® Centaur Syphilis Quality Control Materials are for *in-vitro* diagnostic use to monitor the performance of the Syphilis assay on the ADVIA Centaur® systems. The performance of the SYPH quality control material has not been established with any other Syphilis assay.

Prescription Use __X__ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

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

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) k112343