DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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October 13, 2016

Siemens Healthcare Diagnostics, Inc.
Philip Liu, Ph.D.
Director, Regulatory Affairs and Compliance
511 Benedict Avenue
Tarrytown, NY 10591

Re: K161964
Trade/Device Name: ADVIA Centaur® HAV lgM Assay
Regulation Number: 21 CFR §866.3310
Regulation Name: Hepatitis A virus (HAV) serological assays
Regulatory Class: II
Product Code: LOL
Dated: July 14, 2016
Received: July 18, 2016

Dear Dr. Liu:

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 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" (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 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,

Steven R. Gitterman -S

for Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology 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)*
K161964

Device Name
ADVIA® Centaur HAV IgM (aHAVM) Assay

Indications for Use *(Describe)*

ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems:

The ADVIA Centaur® HAV IgM (aHAVM) assay is an in vitro diagnostic immunoassay for the qualitative determination of IgM response to the hepatitis A virus (HAV) in human pediatric (2 through 21 years) and adult serum or plasma (potassium EDTA, lithium or sodium heparinized) using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems. This assay is intended for use as an aid in the diagnosis of acute or recent infection (usually 6 months or less) with hepatitis A virus.

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, or patients less than 2 years of age.

ADVIA Centaur CP system:

The ADVIA Centaur® HAV IgM (aHAVM) assay is an in vitro diagnostic immunoassay for the qualitative determination of IgM response to the hepatitis A virus (HAV) in human pediatric (2 through 21 years) and adult serum or plasma (potassium EDTA, lithium or sodium heparinized) using the ADVIA Centaur CP system. This assay is intended for use as an aid in the diagnosis of acute or recent infection (usually 6 months or less) with hepatitis A virus.

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, or patients less than 2 years of age.

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.

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510(k) Summary for the

ADVIA® Centaur Hepatitis A IgM (aHAVM) Assay

This 510(k) summary is being submitted in accordance with 21 CFR 807.92.

A. 510(k) Number: K161964

B. Date of Preparation: October 11, 2016

C. Proprietary and Established Names:

ADVIA® Centaur HAV IgM (aHAVM) Assay

D. Applicant:

Siemens Healthcare Diagnostics Inc.,
511 Benedict Ave, Tarrytown, NY 10591
Philip Liu, Director, Regulatory Affairs and Compliance
Office: (914) 524-2443
Fax: (914) 524-3579

E. Regulatory Information:

1. Regulation section: 21 CFR § 866.3310; Hepatitis A virus (HAV) serological assays
2. Classification: Class II
3. Product Code: LOL
4. Panel: Microbiology

F. Purpose of this Submission

The purpose of this submission is to add the pediatric populations to the Intended Use statement of the ADVIA Centaur HAV IgM assay cleared under k081716 (originally approved under PMA, P040018).

G. Predicate Device:

The ADVIA® Centaur HAV IgM Assay is substantially equivalent to the VITROS Immunodiagnostic Products Anti-HAV IgM Reagent Pack cleared under 510(k): k060770

H. Device Description:

The ADVIA Centaur HAV IgM reagent kit contains the following:

- ReadyPack® primary reagent pack containing ADVIA Centaur HAV IgM Lite Reagent, Solid Phase Reagent, and Ancillary Well Reagent
- ReadyPack ancillary pack containing ADVIA Centaur HAV IgM Ancillary Reagent
- ADVIA Centaur HAV IgM Low Calibrator
- ADVIA Centaur HAV IgM High Calibrator
- ADVIA Centaur systems HAV IgM Master Curve cards
- ADVIA Centaur systems HAV IgM Calibrator Assigned Value Card

The HAV IgM ReadyPack consists of the following:

Primary reagent pack

- The Lite Reagent is an anti-HAV mouse monoclonal antibody ($F(ab)_2$ fragment;~0.3 µg/mL) labeled with acridinium ester in buffer with bovine serum albumin, surfactant, sodium azide (<0.1%), and preservatives
- The Solid Phase is streptavidin coated paramagnetic microparticles in buffer with bovine serum albumin, surfactant, sodium azide (< 0.1%), and preservatives
- The Ancillary Well Reagent is inactivated purified hepatitis A virus (<0.1 µg/mL) in buffer with bovine serum albumin, surfactant, sodium azide (<0.1%), and preservatives

Ancillary pack

- The Ancillary Reagent is biotinylated monoclonal mouse anti-human IgM (~0.500 µg/mL) in buffer with bovine serum albumin, mouse IgG, surfactant, sodium azide (< 0.1%), and preservatives

HAV IgM Calibrators

- Processed human plasma negative and positive for anti-HAV IgM antibodies with sodium azide (< 0.1%) and preservatives

I. Intended Use / Indications for Use:

ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems:

The ADVIA Centaur HAV IgM (aHAVM) assay is an in vitro diagnostic immunoassay for the qualitative determination of IgM response to the hepatitis A virus (HAV) in human pediatric (2 through 21 years) and adult serum or plasma (potassium EDTA, lithium or sodium heparinized) using the ADVIA Centaur, ADVIA Centaur XP, and ADVIA Centaur XPT systems. This assay is intended for use as an aid in the diagnosis of acute or recent infection (usually 6 months or less) with hepatitis A virus.

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, or patients less than 2 years of age.

WARNING: This assay has not been FDA cleared or approved for the screening of blood or plasma donors.

United States federal law restricts this device to sale by or on the order of a physician.

ADVIA Centaur CP system:

The ADVIA Centaur HAV IgM (aHAVM) assay is an in vitro diagnostic immunoassay for the qualitative determination of IgM response to the hepatitis A virus (HAV) in human pediatric (2 through 21 years) and adult serum or plasma (potassium EDTA, lithium or sodium heparinized) using the ADVIA Centaur CP system. This assay is intended for use as an aid in the diagnosis of acute or recent infection (usually 6 months or less) with hepatitis A virus.

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, or patients less than 2 years of age.

WARNING: This assay has not been FDA cleared or approved for the screening of blood or plasma donors.

United States federal law restricts this device to sale by or on the order of a physician.

The assay is being marketed on the ADVIA Centaur instrument family members, ADVIA Centaur, ADVIA Centaur XP, XPT, and ADVIA Centaur CP, following FDA's *Replacement Reagent and Instrument Family Policy* (December 11, 2003). Additionally, the ADVIA Centaur XPT system has been reviewed under 510(k) k141999.

J. Substantial Equivalence Information:

Both the ADVIA Centaur HAV IgM and the VITROS Immunodiagnostic Products Anti-HAV IgM Reagent Pack (cleared under 510(k) k060770) employ prepackaged reagents for use on automated test systems. The Intended Use / Indications for Use, Assay Principle and reagent formulations (use of mouse monoclonal antibodies) are very similar. The major differences between the Device and the Predicate Device are the standardization / traceability and the differences in conjugation of the monoclonal antibodies. A comparison of the important similarities and differences of these assays is shown in the following tables:

Assay:

Similarities:

Item	Modified Device: ADVIA Centaur HAV IgM Assay	Predicate Device: VITROS Anti-HAV IgM Reagent
Intended Use	For the qualitative determination of IgM response to hepatitis A virus (anti-HAV IgM) in human pediatric (2 through 21 years) and adult samples	For the qualitative determination of IgM antibodies to hepatitis A virus (anti-HAV IgM) in human adult and pediatric samples
Indications for Use	This assay is intended for use as an aid in the diagnosis of acute or recent infection (usually 6 months or less) with hepatitis A virus.	The assay is indicated for testing specimens from individuals who have signs and symptoms consistent with acute hepatitis. Assay results, in conjunction with other clinical information, may be used for the laboratory diagnosis of individuals with acute or recent hepatitis A.
Sample type	Serum and Plasma	Same
Measurement	Qualitative	Same
Assay Principle	IgM capture immunoassay	Same
Technology	Chemiluminescence	Same

Differences:

Item	Modified Device: ADVIA Centaur HAVT Assay	Predicate Device: VITROS Anti-HAV IgM Reagent
Standardization / Traceability	The cutoff for the ADVIA Centaur HAV IgM assay was verified based on results of Receiver-Operator characteristics (ROC) Curve and clinical agreement generated from the clinical studies.	Traceable to an in-house reference calibrator which has been value assigned to optimize the clinical sensitivity and specificity performance.
Detection Antibody	Mouse monoclonal anti-HAV antibody Fab fragments labeled with acridinium ester	Mouse monoclonal anti-HAV antibody labeled with horseradish peroxidase (HRP)
Capture Antibody	Mouse monoclonal to anti-human IgM antibody labeled with biotin	Mouse monoclonal to anti-human IgM antibody labeled with biotin

K. Standard/Guidance Document Referenced (if applicable):

- None Referenced

L. Test Principle

The ADVIA Centaur HAV IgM assay is an IgM capture immunoassay using a 2-pass format. In the first pass the sample is diluted using Multi-Diluent 2. After sample dilution biotinylated anti-human IgM monoclonal antibody is added to the cuvette binding IgM from the diluted patient sample. The IgM complex is then captured by the addition of streptavidin coated magnetic latex particles (MLP). The IgM-MLP is washed and resuspended. In the second pass the anti-HAV IgM captured on the Solid Phase is detected by the sequential addition of HAV antigen and acridinium ester-labeled mouse anti-HAV antibody.

M. Performance Characteristics

The following comparison study was performed to demonstrate that the pediatric and adolescent populations can be used in the ADVIA Centaur HAV IgM assay:

One hundred and thirty-two (132) pediatric serum samples (male and female, age range from 2 to 21 years) from suspected positive or high risk population were evaluated with the ADVIA Centaur HAV IgM assay and another commercially available assay.

The percent agreement (including 95% confidence intervals) of results for reactive and nonreactive samples between the ADVIA Centaur HAVM and comparative assay for the pediatric population is shown in the following table:

Results of Pediatric Population (2 to 21 years) Comparison Study

	Comparative anti-HAV IgM Assay			
ADVIA Centaur Anti-HAV IGM Assay	Reactive	Borderline Reactive	Non-reactive	Total
Reactive	30	0	0	30
Equivocal	0	1	1	2
Non-reactive	1	2*	97	100
Total:	31	3	98	132

% Positive Agreement = 90.9% (30/33)

95% Confidence Interval = 75.67% to 98.08%

% Negative Agreement = 98.98% (97/98)

95% Confidence Interval = 94.45% to 99.97%

* Included in the total number of samples (n=33) in the calculation of % Positive Agreement

The inclusion of pediatric populations in the ADVIA Centaur HAV IgM assay intended use does not necessitate the collection of additional analytical performance data since there was no change to the assay. All performance data are cross-referenced to the original Premarket Approval for the ADVIA Centaur HAV IgM assay on the ADVIA Centaur systems (P040018) and to the clearance in 510(k) number k081716.

Specifically, the following studies are not needed for the purpose of this submission:

- Precision/Reproducibility
- Calibrator/Assay Traceability
- Calibrator/Assay Stability
- Assay Cut-off
- Method Comparison
- Matrix Comparison
- Analytical Sensitivity
- Analytical Specificity

N. Conclusions

Comparative testing of the ADVIA Centaur HAV IgM assay with the addition of the pediatric populations is substantially equivalent in principle and performance to the Predicate Device VITROS Immunodiagnostic Products Anti-HAV IgM Reagent Pack cleared under 510(k) number k060770.