JAN 2 4 2014

510(k) Summary of Safety and Effectiveness for the ADVIA® Chemistry Fructosamine (FRUC) Assay and Calibrator

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: k131307

B. Date of Preparation: May 3, 2013

C. Proprietary and Established Names:

ADVIA® Chemistry Fructosamine (FRUC) Assay
ADVIA® Chemistry Fructosamine Calibrator

D. Applicant

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E. Regulatory Information:

Reagent

1. Regulation section:
   21 CFR §864.7470, Glycosylated hemoglobin assay
2. Classification:
   Class II
3. Product Code:
   LCP
4. Panel:
   Hematology (81)

Calibrator

1. Regulation section:
   21 CFR §862.1150, Calibrator, secondary
2. Classification:
   Class II
3. Product Code:
   JIT
4. Panel:
   Clinical Chemistry (75)

F. Predicate Device:

Reagents:

1. Device Name:

Diazyme Glycated Serum Protein Assay
2. Common Name:
Diazyme Glycated Serum Protein Assay
3. 510(k) Number:
k042193
4. Manufacturer:
Diazyme Laboratories

Calibrators:
1. Device Name:
Randox Fructosamine Calibrator
2. Common Name:
Randox Fructosamine Calibrator
3. 510(k) Number:
k023763
4. Manufacturer:
Randox Laboratories, Ltd.

G. Intended Use and Indication for Use:

ADVIA Chemistry Fructosamine (FRUC) Assay
For *in vitro* diagnostic use in the quantitative measurement of glycated protein (fructosamine) in human serum or plasma on the ADVIA® Chemistry systems. Measurement of fructosamine is representative of blood glucose levels over the preceding 2-3 weeks, and is useful for monitoring diabetic patients.

ADVIA Chemistry Fructosamine Calibrator
For *in vitro* diagnostic use in the calibration of the ADVIA® Chemistry Fructosamine (FRUC) assay on ADVIA Chemistry systems.

H. Device Description:

The ADVIA® Chemistry Fructosamine reagents are ready-to-use liquid packaged for use on ADVIA® 1650 Chemistry system. The reagents are supplied as 100 tests/wedge, with two (2) wedges in each kit.

- Reagent 1 (R1) contains Tris Buffer (0.2 mol/L, pH 8.0), Proteinase-K (≥ 1 kU/mL) 4-Aminoantipyrine (5 mmol/L) and Stabilizers.
- Reagent 2 (R2) contains Tris Buffer (0.2 mol/L, pH 8.65), Fructosaminase (≥ 0.5 kU/mL), Peroxidase (horseradish) (0.5 kU/mL) N-ethyl-N-sulphohydroxypropyl-m-toluidine (TOOS) (10 mmol/L) and Stabilizers.

The ADVIA® Chemistry Fructosamine Calibrator is a single analyte and single level calibrator. It is lyophilized human serum containing pure fructosamine antigen. There are three (3) vials in each kit. Each vial contains 0.08g. The volume per vial (after reconstitution with deionized water) is 1.0 mL.

I. Test Principle:

In the ADVIA® Chemistry Fructosamine Assay, Reagent 1 contains proteinase K, which digests the glycated protein to yield glycated protein fragments. Fructosaminase in Reagent 2

oxidizes the ketoamine bond of the glycated protein fragments. As a result hydrogen peroxide is released and it is involved in a colorimetric Trinder end-point reaction. The amount of color developed and measured at 596 nm is proportional to the concentration of glycated protein in the sample.

J. Substantial Equivalence Information:

1. Predicate device name:
   Reagent: Diazyme Glycated Serum Protein Assay;
2. Calibrator: Randox Fructosamine Calibrator
   Predicate K number:
3. Reagent: k042193
   Calibrator: k023763

Comparison with predicate:

Assay:

Similarities and Differences: Assay		
ITEM	**NEW DEVICE: ADVIA® Chemistry Fructosamine (FRUC) Assay**	**PREDICATE DEVICE:** Diazyme Glycated Serum Protein Assay
Intended Use/Indications for Use	For *in vitro* diagnostic use in the quantitative measurement of glycated protein (fructosamine) in human serum or plasma on the ADVIA® Chemistry systems. Measurement of fructosamine is representative of blood glucose levels over the preceding 2-3 weeks, and is useful for monitoring diabetic patients.	Same (for the quantitative determination of glycated serum proteins (GSP; glycated albumin; fructosamine). The measurement of glycated serum proteins is useful for monitoring diabetic patients.
Instrument used	ADVIA® 1650 Chemistry system	Clinical Chemistry analyzer
Measurement	Quantitative	Same
Specimen types	Human Serum and plasma (Lithium heparin, potassium EDTA)	Serum
Reference range	122–236 µmol/L	Same
Format	Liquid	Same
Analytical Range	30–1000 µmol/L	21-1354 µmol/L
Assay Principle/ Methodology	Enzymatic reaction	Same

Calibrator:

Similarities and Differences: Calibrator		
Item	**NEW DEVICE: ADVIA® Chemistry Fructosamine Calibrator**	**PREDICATE DEVICE: Randox Fructosamine Calibrator**
Intended Use	For *in vitro* diagnostic use in the calibration of the ADVIA® Chemistry	**Same-** Intended for *in vitro* use in

	Fructosamine (FRUC) assay on ADVIA® Chemistry systems.	the calibration of Fructosamine on clinical chemistry systems.
Form	Lyophilized	Same
Analyte source	Derived from human source	Same
Levels	Single	Same
Fill Volume	0.08g→1.0mL reconstituted	Same
Storage	2–8°C	Same

K. Standard/Guidance Document Reference

a. Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition(CLSI EP7-A2)
b. Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition (CLSI EP17-A2)
c. Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition (CLSI EP5-A2)

L. Performance Characteristics

The following data represent typical performance for the ADVIA® Chemistry Fructosamine Assay and were collected on ADVIA® 1650 Chemistry system. Substantial equivalence was demonstrated by testing several performance characteristics including imprecision, linearity/assay reportable range, limit of detection, method comparison and analytical specificity. All of the evaluation studies gave acceptable results when compared to the predicate device. These studies support that the ADVIA® Chemistry Fructosamine Assay and ADVIA® Chemistry Fructosamine Calibrator when tested on the ADVIA® 1650 Chemistry system are substantially equivalent to the Diazyme Glycated Serum Protein Assay and Randox Fructosamine Calibrator that are currently marketed.

I. **Imprecision**

Within-Run and Total Precision were established by assaying three samples. Each sample was assayed 2 replicates per run, 2 runs per day, for at least 20 days. Precision estimates were computed according to CLSI document EP5-A2, *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline.*

Sample	N	Mean (µmol/L)	Within Run		Between Run		Between Day		Total	
			SD	CV	SD	CV	SD	CV	SD	CV
Serum Pool	80	39	1.1	2.8	0.8	1.9	0	0	1.4	3.5
Serum Pool	80	70	0.5	0.7	1.2	1.7	1.6	2.2	2.0	2.9
Serum Pool	80	126	0.7	0.5	1.5	1.2	1.4	1.1	2.2	1.7
Serum Control	80	150	0.5	0.3	1.1	0.7	1.8	1.2	2.2	1.4
Serum Pool	80	273	0.9	0.3	1.9	0.7	1.6	0.6	2.6	1.0
Serum Control	80	429	1.1	0.3	2.2	0.5	3.5	0.8	4.2	1.0
Serum Pool	80	540	1.3	0.2	3.2	0.6	3.3	0.6	4.7	0.9
Serum Pool	80	731	1.9	0.3	1.9	0.3	5.2	0.7	5.8	0.8

II. **Linearity/assay reportable range**

Linearity was assessed by assaying equally spaced dilutions across the measuring range. The low end of the assay range is calculated based on the Limit of Quantitation. The high

end of the assay range is based on the linearity calculation. The ADVIA® Chemistry Fructosamine Assay on ADVIA® 1650 Chemistry system is linear from 30–1000 µmol/L with a deviation from linearity of ≤ 10%.
Results of the linear regression equation are as follows:
Observed FRUC (µmoL/L) = 0.995 * Expected FRUC (µmoL/L) + 4.12, r = 1.000

III. **Limit of detection**
The ADVIA® Chemistry Fuctosamine Assay estimations of the Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) were performed according to CLSI document EP17-A2, *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition* using several serum pools with fructosamine concentration and 160 replicates of blank ("zero") serum pool.

The Limit of Blank (LoB) is the highest measurement result that is likely to be observed on a blank sample. The LoB for the ADVIA® Chemistry Fructosamine Assay is 15 µmol/L on ADVIA® 1650 Chemistry system.

The Limit of Detection (LoD) is the smallest amount that this assay can reliably detect to determine presence or absence of an analyte. The LoD for the ADVIA® Chemistry Fuctosamine Assay is 21 µmol/L on ADVIA® 1650 Chemistry system.

LoB and LoD values are determined with proportions of false positives (α) less than 5% and false negatives (ß) less than 5%, based on 320 determinations with 160 blank and 160 low level sample replicates for the ADVIA® 1650 Chemistry system.

The Limit of Quantitation (LoQ) is based on 160 determinations and a total error goal of 30.0% calculated using the Westgard model. The LoQ for the ADVIA® Chemistry Fuctosamine Assay is 30 µmol/L on ADVIA® 1650 Chemistry system.

IV. **Method comparison with predicate device:**
The performance of the ADVIA® Chemistry Fructosamine Assay on ADVIA® 1650 Chemistry system (y) was compared with the performance of Diazyme Glycated Serum Protein Assay on Hitachi 717 (x).

One hundred and thirteen (113) serum samples were tested. Three (3) samples were not included in calculations being out if the assay range. The sample results ranged from 47–995 µmol/L fructosamine (x), and gave a correlation coefficient (r) of 0.99. The ADVIA® Chemistry Fructosamine assay result was calculated using least squares linear regression (first replicate) is as follows:

Regression Equation	Slope (95% CI)	Intercept (95% CI)	r	Sample Range
y = 0.99x - 13.1 µmol/L	0.99 – 1.00	-17.2 – -9.0	0.99	47 - 995 µmol/L

V. Matrix comparison

The performance of the plasma samples (y) on ADVIA® Chemistry Fructosamine Assay on was compared with the performance of serum samples (x) on ADVIA® 1650 Chemistry system.

One hundred and fifty two (152) Lithium Heparin plasma samples and one hundred twenty eight (128) potassium EDTA plasma samples were tested vs. serum; the sample results ranged from 38–940 µmol/L fructosamine (x). The ADVIA® Chemistry Fructosamine Assay result calculated using least squares linear regression (first replicate) is as follows:

Matrix	Regression Equation	Slope (95% CI)	Intercept (95% CI)	r	Sample Range
Lithium Heparin (Plasma)	y = 1.00x + 3.5	0.98 to 1.02	-2.1 to 9.0	0.995	38 – 940 µmol/L
Potassium EDTA (Plasma)	y = 1.00x – 4.6	0.98 to 1.02	-11.2 to 2.0	0.994	38 – 940 µmol/L

VI. Analytical specificity

Interferences from various substances (see table below) were evaluated using a significance criterion of >10% bias. Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% is considered interference.

Interferent	Interferent Level	Fructosamine Sample Concentration	Interference*
Bilirubin (conjugated)	5 mg/dL (86 µmol/L)	165 µmol/L	NSI
	10 mg/dL (171 µmol/L)	165 µmol/L	-18.3%
	5 mg/dL (86 µmol/L)	263 µmol/L	NSI
	10 mg/dL (171 µmol/L)	263 µmol/L	-13.6%
Bilirubin (unconjugated)	5 mg/dL (86 µmol/L)	165 µmol/L	NSI
	10 mg/dL (171 µmol/L)	165 µmol/L	-16.2%
	10 mg/dL (171 µmol/L)	264 µmol/L	NSI
	15 mg/dL (257 µmol/L)	264 µmol/L	-12.4%
Hemolysis	250 mg/dL (2.5 g/L)	154 µmol/L	NSI
	500 mg/dL (5.0 g/L)	154 µmol/L	-11.3%
	750 mg/dL (7.5 g/L)	253 µmol/L	NSI
	1000 mg/dL (10.0 g/L)	253 µmol/L	-13.7%
Lipemia (from Triglyceride Concentrate)	1000 mg/dL (11.3 mmol/L)	156 µmol/L	NSI
	1000 mg/dL (11.3 mmol/L)	256 µmol/L	NSI
Ascorbic Acid	10 mg/dL (568 µmol/L)	156 µmol/L	NSI
	15 mg/dL (852 µmol/L)	156 µmol/L	+13.2%
	20 mg/dL (1136 µmol/L)	250 µmol/L	NSI
Glucose	2800 mg/dL (155 mmol/L)	154 µmol/L	NSI
	2800 mg/dL (155 mmol/L)	251 µmol/L	NSI
Uric Acid	50 mg/dL (2975 µmol/L)	159 µmol/L	NSI
	50 mg/dL (2975 µmol/L)	251 µmol/L	NSI
Albumin	6.1 g/dL (61 g/L)	132 µmol/L	NSI
Total Protein	8.4 g/dL (84 g/L)	489 µmol/L	NSI

* NSI = No Significant Interference. A percentage effect ± 10% is considered a significant interference.

VII. **Reagent and Calibrator Stability**

Reagent: for opened products, once placed on the system reagents are stable for 60 days. The shelf life of the ADVIA Chemistry Fructosamine Reagent is 12 months at 2-8°C. For unopened product, see the expiration date on the reagent carton.
Calibrator: for opened products, once the cap is removed, assigned values are stable for 28 days when recapped immediately after use and stored at 2-8°C. The shelf life of the ADVIA Chemistry Fructosamine Calibrator is 12 months at 2-8°C. For unopened product, see the expiration date on the calibrator carton.

VII. **Value Assignment**

The ADVIA Chemistry FRUC assay is traceable to an internal standard. Assigned values of the ADVIA Chemistry Fructosamine Calibrator are traceable to this standardization. The value assignment is carried out by a nested testing protocol using one lot of reagent on one ADVIA® 1650 Chemistry system with ten (10) replicates of the Master Lot and Test Lot calibrators in the same worklist. The Test Lot values are adjusted with a ratio derived from the Master Lot Calibrator assigned value (Target value) and the mean recovery of the Master Lot Calibrator values (observed) according to the following equation: Test Lot assigned value = (Master Calibrator Target value / Mean Recovery of the Master Lot Calibrator observed) * Mean Recovery of Test Lot observed.

VII. **Clinical Studies**

Not applicable.

VIII. **Clinical cut-off**

Not applicable.

M. Conclusion

The ADVIA® Chemistry Fructosamine Assay on ADVIA® 1650 Chemistry system is substantially equivalent in principle and in performance to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Diazyme Glycated Serum Protein Assay (k042193).

The ADVIA® Chemistry Fructosamine Calibrator on ADVIA® 1650 Chemistry system is substantially equivalent n principle and in performance to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the currently marketed Randox Fructosamine Calibrator (k023763).

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 24, 2014

SIEMENS HEALTHCARE DIAGNOSTICS, INC.
KIRA GORDON
SR. REGULATORY TECHNICAL SPECIALIST
511 BENEDICT AVE
TARRYTOWN NY 10591

Re: K131307
Trade/Device Name: ADVIA® Chemistry Fructosamine (FRUC) Assay
ADVIA® Chemistry Fructosamine Calibrator
Regulation Number: 21 CFR 864.7470
Regulation Name: Glycosylated hemoglobin assay
Regulatory Class: II
Product Code: LCP, JIT
Dated: December 6, 2013
Received: December 9, 2013

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. 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,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology 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)*
k131307

Device Name
ADVIA® Chemistry Fructosamine (FRUC) Assay; ADVIA® Chemistry Fructosamine Calibrator

Indications for Use *(Describe)*
The ADVIA® Chemistry Fructosamine (FRUC) Assay

For in vitro diagnostic use in the quantitative measurement of glycated protein (fructosamine) in human serum or plasma on the ADVIA® Chemistry systems. Measurement of fructosamine is representative of blood glucose levels over the preceding 2-3 weeks, and is useful for monitoring diabetic patients.

ADVIA® Chemistry Fructosamine Calibrator

For in vitro diagnostic use in the calibration of the ADVIA® Chemistry Fructosamine (FRUC) assay on ADVIA® Chemistry systems.

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)*

Stayce Beck

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