DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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April 27, 2016

SIEMENS HEALTHCARE DIAGNOSTICS, INC.
LAURA J. DUGGAN
REGULATORY TECHNICAL SPECIALIST
500 GBC DRIVE, PO BOX 6101 MS 514
NEWARK, DE 19711 US

Re: K160202
Trade/Device Name: Trinidad CH Vancomycin (Vanc)
Trinidad CH Drug 3 Calibrator (DRUG3 CAL)
Regulation Number: 21 CFR 862.3950
Regulation Name: Vancomycin test system
Regulatory Class: Class II
Product Code: LEH, DLJ
Dated: January 27, 2016
Received: January 28, 2016

Dear Ms. Duggan,

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 regulation (21 CFR Part 801), 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" (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 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,

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 below.

510(k) Number *(if known)*
k160202

Device Name
Trinidad CH Vancomycin (Vanc)
Trinidad CH Drug 3 Calibrator (DRUG3 CAL)

Indications for Use *(Describe)*
The Trinidad CH Vancomycin (Vanc) assay is for in vitro diagnostic use in the quantitative measurement of vancomycin in human serum or plasma on the Trinidad CH System. Vanc test results may be used in the diagnosis and treatment of vancomycin overdose and in monitoring levels of vancomycin to ensure appropriate therapy.

The Trinidad CH Drug 3 Calibrator (DRUG3 CAL) is intended for in vitro diagnostic use in the calibration of Vancomycin (Vanc) on the Trinidad CH System.

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

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

ASSIGNED 510(K) NUMBER

The assigned 510(k) number is _k160202____.

APPLICANT AND DATE

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March 29, 2016

MANUFACTURER

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REGULATORY INFORMATION

Regulatory Submission for the Trinidad CH Vancomycin (Vanc) and Trinidad CH Drug 3 Calibrator (DRUG3 CAL)

Common Name:	Clinical Toxicology Test Systems	Clinical Toxicology Test Systems
Proprietary Name:	Trinidad CH Vancomycin (Vanc) Assay	Trinidad CH Drug 3 Calibrator (DRUG3 CAL)
Classification Name:	Vancomycin test system	Clinical Toxicology Calibrator
Regulation Number:	21CFR862.3950	21CFR862.3200
Classification:	Class II	Class II
Product Code:	LEH	DLJ
Panel:	Toxicology	Toxicology
Predicate Device:	Vancomycin Flex Reagent Cartridge (k963267)	Dimension Drug Calibrator II (k033809)

DEVICE DESCRIPTION

TRINIDAD CH VANCOMYCIN (VANC)

The Trinidad CH Vancomycin (Vanc) assay is based on a homogeneous particle enhanced turbidimetric inhibition immunoassay (PETINIA) technique which uses a synthetic particle-vancomycin conjugate (PR) and monoclonal vancomycin specific antibody (Ab). Vancomycin present in the sample competes with vancomycin on the particles for available antibody, thereby decreasing the rate of aggregation. Hence, the rate of aggregation is inversely proportional to the concentration of vancomycin in the sample. The rate of aggregation is measured using bichromatic turbidimetric readings at 545 nm and 694 nm.

Reaction Equation

Serum and lithium heparin plasma specimens may be used. The reagent is stored unopened at 2 – 8 °C and is stable for use on system for 30 days. Calibration is performed every 30 days for a reagent lot or every 7 days for an individual pack.

TRINIDAD CH DRUG3 CALIBRATOR (DRUG3 CAL)

The Trinidad CH Drug 3 Calibrator (DRUG3 CAL) is a 5 level calibrator product prepared from bovine serum base product. The product is stored at 2 – 8 °C. The Trinidad CH Drug 3 Calibrator is stable for 15 days at 2 – 8 °C after being opened and securely recapped.

INTENDED USE/INDICATIONS FOR USE

TRINIDAD CH VANCOMYCIN (VANC)

The Trinidad CH Vancomycin (Vanc) assay is for *in vitro* diagnostic use in the quantitative measurement of vancomycin in human serum or plasma on the Trinidad CH System. Vanc test results may be used in the diagnosis and treatment of vancomycin overdose and in monitoring levels of vancomycin to ensure appropriate therapy.

TRINIDAD CH DRUG3 CALIBRATOR (DRUG3 CAL)

The Trinidad CH Drug 3 Calibrator (DRUG3 CAL) is intended for *in vitro* diagnostic use in the calibration of Vancomycin (Vanc) on the Trinidad CH System.

COMPARISON OF TECHNOLOGICAL CHARACTERISTICS

Below is a features comparison for the Trinidad CH system Vancomycin assay and the DRUG3 calibrator vs. their predicates:

Feature	**Predicate Device:** Dimension® VANC Flex® reagent Cartridge (k963267)	**New Device:** Trinidad CH Vancomycin (VANC)
Intended Use :	The VANC assay used on the Dimension clinical chemistry system is an *in vitro* diagnostic test intended to measure vancomycin, a glycopeptide antibiotic in human serum or plasma.	For *in vitro* diagnostic use in the quantitative measurement of vancomycin in human serum or plasma on the Trinidad CH System.
Indications for Use:	VANC test results may be used in the diagnosis and treatment of vancomycin overdose and in monitoring levels of vancomycin to ensure appropriate therapy.	Same
Device Technology:	Homogeneous particle enhanced turbidimetric inhibition immunoassay (PETINIA) technique	Same
Sample Type:	Serum/ Lithium Heparin plasma	Same
Therapeutic Interval:	Peak Intervals: Samples from adult volunteers drawn two hours after the completion of a 60 minute infusion of vancomycin ranged from 18 – 26 µg/mL. Samples drawn one hour after the completion of a 60	Same

	minute vancomycin infusion ranged from 25 – 40 µg/mL. Samples drawn 30 minutes after the completion of a 60 minute infusion of vancomycin ranged from 30 – 40 µg/mL. Trough Intervals: Samples should be drawn just before the next dose. A trough interval of 5 – 10 µg/mL is recommended.	
Standardization:	Traceable to United States Pharmacopeia (USP) standards.	Same
Calibration Frequency:	30 days	Same
Analytical Measuring Interval:	0.0 – 50.0 µg/mL	3.0–50.0 µg/mL
Interferences:	Bilirubin (Unconjugated) – 80 mg/dL Lipemia (Intralipid®) – 200 mg/dL Hemoglobin – 1000 mg/dL	Bilirubin (Conjugated & Unconjugated) – 20 mg/dL Lipemia (Intralipid®) – 1000 mg/dL Hemoglobin – 600 mg/dL
Calibrators:	Drug Calibrator II (k033809)	Drug 3 Calibrator

Feature	**<u>Predicate Device:</u> Dimension Drug Calibrator II (k033809)**	**<u>New Device:</u> Trinidad CH Drug 3 Calibrator (DRUG3 CAL)**
Calibrator Matrix:	Bovine Serum Base	Same
Calibrator Form:	Liquid	Same
Number of Calibrator Levels:	Five	Same

SUMMARY OF PERFORMANCE TESTING

Assay performance comparison results for the Trinidad CH Vancomycin (Vanc) with the Trinidad CH Drug 3 Calibrator were obtained by processing the appropriate body fluids. Summary statistics for each are provided. These data demonstrate substantial equivalency of the Trinidad CH Vancomycin (Vanc) with the Trinidad CH Drug 3 Calibrator versus the predicate devices. The following data represent typical assay performance.

DETECTION LIMIT

The Limit of Blank (LoB) and Limit of Detection (LoD) were evaluated in accordance with CLSI EP17-A2 Protocols for Determination of Limits of Detection and Limits of Quantitation: Approved Guideline.

Assessment of LoB was the 95th percentile of all values (sorted from lowest to highest), using non-parametric approach.

LoB Rank Position = 0.5 +0.95*B, where B=total reps=60; Rank = 57.5

Trinidad CH Vancomycin (Vanc) - Limit of Detection Results		
Limit	Protocol	Result
LoB	4 samples with no analyte (bovine serum base) were tested (N=5) for 3 days, one run per day, 3 reagent lots,	0.1 µg/mL
LoD	4 low serum samples were tested (N=5) for 3 days, one run per day, 3 reagent lots	0.2 µg/mL

The nonparametric approach described in EP17-A2 was followed to determine the Limit of Detection.

LOQ

The Limit of Quantitation (LoQ) for serum was determined as described in CLSI Document EP17-A2. Total Error is calculated using: TE = bias + 2 * SD.

Four low serum samples were processed on three reagent lots for three days, on one instrument for a total of 60 measurements per reagent lot. The measured LoQ was 2.8 µg/mL in support of the LoQ claim of 3.0 µg/mL based a total of 180 determinations with a total error of ≤ 20%.

LINEARITY STUDY

Linearity was evaluated with 10 samples which spanned the assay measuring interval. Each was prepared by mixing high and low concentration samples across the measurement interval as described in CLSI Evaluation of the Linearity of Quantitative Measurement Procedure (EP06-A). The high sample was prepared by spiking native serum with purified vancomycin hydrochloride. The low sample was normal human serum. Six replicates were measured for each sample. The mean of these replicates was used for the calculations.

The assay was considered linear across the measuring interval if the nonlinear coefficients are nonsignificant (all p values are ≥ 0.05). If one or more of them are significant ($p < 0.05$), then the allowable bias is ≤ 0.5 µg/mL or 10%, whichever is greater.

Vancomycin Linearity, results in µg/mL

Reagent Lot 1							
Level	Lot 1 Expected (µg/mL)	Lot 1 Observed (µg/mL)	Predicted (µg/mL)	Absolute Bias (µg/mL)	% Bias	Allowable Bias (µg/mL)	Observed Bias ≤ Allowable Bias Pass/Fail
1	0.9	0.9	0.7	0.2	N/A	0.5	Pass
2	3.0	3.0	2.9	0.1	N/A	0.5	Pass
3	7.2	7.0	7.1	-0.1	N/A	0.5	Pass
4	13.5	13.1	13.4	-0.3	-2.3	0.7	Pass
5	19.7	19.7	19.7	0.0	-0.2	1.0	Pass
6	26.0	25.9	26.1	-0.2	-0.7	1.3	Pass
7	32.3	32.3	32.4	-0.1	-0.3	1.6	Pass
8	38.6	39.1	38.7	0.4	0.9	1.9	Pass
9	44.8	45.3	45.1	0.2	0.5	2.2	Pass
10	51.1	51.1	51.4	-0.3	-0.6	2.6	Pass

PRECISION STUDIES

Precision testing was performed in accordance with CLSI EP05-A3 Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline –

Third Edition. Precision was tested n = 2 replicates, two times a day for at least 20 days for a total of 80 replicates with controls, serum and plasma pools on one instrument. Analysis of variance (ANOVA) was used to evaluate the data consistent with the recommendations of EP05-A3. The data are summarized in the following table.

Specimen Type	N	Mean µg/mL (µmol/L)	Repeatability		Within-Lab	
			SD[a] µg/mL (µmol/L)	CV[b] (%)	SD[a] µg/mL (µmol/L)	CV[b] (%)
Serum QC	80	6.4 (4.4)	0.16 (0.11)	2.6	0.18 (0.12)	2.7
Serum	80	11.2 (7.7)	0.20 (0.14)	1.8	0.23 (0.16)	2.0
Serum QC	80	17.5 (12.1)	0.28 (0.19)	1.6	0.35 (0.24)	2.0
Serum	80	32.7 (22.6)	0.46 (0.32)	1.4	0.67 (0.46)	2.0
Plasma	80	45.8 (31.6)	0.78 (0.54)	1.7	0.83 (0.57)	1.8

[a] SD = standard deviation

[b] CV = coefficient of variation

INTERFERENCES

CLSI EP7-A2 was followed for the interference testing. The interference study was conducted using a “paired difference worst case scenario” approach where these compounds were spiked into fresh sample pools containing either low or high levels of measurand in serum pools.

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. Dilution studies were conducted to determine the level at which the spiked substance no longer displayed significant interference. Dilution studies were conducted at two analyte concentrations, if both sample pools show significant interference. This study was conducted as needed for both serum pools.

Approximate Concentration (within 10%) of Analytes in Test Pools			
Analyte	Matrix	Low	High
Vanc	Serum	10.0 µg/mL	40.0 µg/mL

No interference was detected at the following analyte concentrations.

Interferent Concentration

Hemoglobin 600 mg/dL
Conjugated Bilirubin 20 mg/dL
Unconjugated Bilirubin 20 mg/dL
Lipemia (Intralipid) 1000 mg/dL

Vancomycin crystalline degradation product (CDP-1) at 20 µg/mL demonstrates cross-reactivity at 0 and 10 µg/mL Vanc of 21.0% and 19.1% respectively.

METHOD COMPARISON

The predicate device selected for the method comparison study was the Dimension RxL VANC assay cleared under K963267. Remnant de-identified samples were tested. No patient history information was obtained on these samples. Inclusion/exclusion data criteria are not applicable. The study included native, spiked, and diluted samples to properly span the assay intervals.

These studies were conducted internally by Siemens Healthcare Diagnostic Inc. R&D organization personnel. The personnel conducting the study were laboratory technicians with training similar to personnel who would conduct the tests in a hospital laboratory setting. They were trained on the operation of both the device and the predicate device. A split sample method comparison, following EP09-A3, demonstrated good agreement between the Trinidad CH Vancomycin (Vanc) and the predicate Dimension RxL VANC assay with patient samples.

The results across the full assay intervals were analyzed by Deming regression. One replicate of each sample was tested and used in the analysis.

Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sample Interval
Serum	Dimension® RxL VANC	100	0.997	y = 1.04x – 1.04 µg/mL	4.4–48.1 µg/mL

MATRIX EQUIVALENCY

Serum and lithium heparin plasma equivalency was demonstrated by testing sixty matched samples. Some samples were diluted with water or spiked with vancomycin to obtain samples spanning the assay measuring intervals. The table below summarizes the Deming linear regression statistics. The results across the full assay intervals were analyzed by Deming regression. One replicate of each sample was tested and used in the analysis.

Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sample Interval
Plasma (Lithium heparin)	Trinidad CH Vanc – Serum	60	0.990	y = 1.00x + 0.49 µg/mL	4.0–43.3 µg/mL

THERAPEUTIC INTERVAL

The therapeutic intervals are cited from the literature[1,2]:

There is great disparity in vancomycin therapeutic intervals, especially with peak therapeutic intervals. Factors that might affect peak therapeutic intervals include dosage regimen and timing of sample collection.

Vancomycin levels in renal dialysis patients, burn patients and intravenous drug abusers should be closely monitored.

Peak Intervals: Samples from adult volunteers drawn two hours after the completion of a 60 minute infusion of vancomycin ranged from 18 – 26 µg/mL.

Samples drawn one hour after the completion of a 60 minute vancomycin infusion ranged from 25 – 40 µg/mL.

Samples drawn 30 minutes after the completion of a 60 minute infusion of vancomycin ranged from 30 – 40 µg/mL.

Trough Intervals: Samples should be drawn just before the next dose. A trough intervals of 5 – 10 µg/mL is recommended.
Note: The physician must ultimately determine the most appropriate vancomycin therapeutic interval for each patient.

1. Burtis CA, Ashwood ER, Bruns DE. Tietz Textbook of Clinical Chemistry and Molecular Biology, Fourth Edition, Elsevier Saunders, St. Louis, MO; pp. 1253 (clinical significance), pp. 2315 (reference values).

2. Finn AL, Taylor WJ. Individualizing Drug Therapy, Practical Applications of Drug Monitoring. New York: Gross, Townsend, Frank, Inc., 1981: 87-108.

CONCLUSION

The Trinidad CH Vancomycin (Vanc) and the Trinidad CH Drug 3 Calibrator are substantially equivalent to the Dimension® VANC Flex® reagent Cartridge and the Dimension Drug Calibrator II in principle and performance based on the similarity of device designs and function demonstrated through method comparison and other performance attributes.