

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE**

A. 510(k) Number: K032811

B. Analyte: Vancomycin

C. Type of Test:

Quantitative assay utilizing recombinant DNA technology to produce a unique homogenous enzyme immunoassay.

D. Applicant: Microgenics Corporation

E. Proprietary and Established Names: Microgenics Cedia® Vancomycin Assay

F. Regulatory Information:

1. Regulation section: 21 CFR §862.3950 Vancomycin test system
2. Classification: Class II
3. Product Code: LEH
4. Panel: Toxicology (91)

G. Intended Use:

1. Indication(s) for use:

The CEDIA® Vancomycin Assay is a homogenous immunoassay intended for in vitro diagnostic use in the quantitative determination of vancomycin in human serum or plasma.

2. Special condition for use statement(s):

The incidence of patients having antibodies to E. coli β -galactosidase is extremely low. However, some samples contain such antibodies can result in artificially high results that do not fit the clinical profile.

3. Special instrument Requirements: None

H. Device Description:

I. Substantial Equivalence Information:

1. Predicate device name(s): Abbott Diagnostics AxSYM® Vancomycin II
2. Predicate K number(s): K955851

3. Comparison with predicate:

Device Characteristics	Subject Device	Predicate Device (K955851)
Intended Use	The CEDIA® Vancomycin Assay is a homogenous enzyme immunoassay intended for in vitro diagnostic use in the quantitative determination of vancomycin in human serum or plasma.	Axsym® Vancomycin II is a reagent system for the quantitative measurement of vancomycin, an antibiotic drug, in serum or plasma. The measurements obtained are used in the diagnosis and treatment of vancomycin overdose and in monitoring levels of vancomycin to ensure appropriate therapy.
Analyte	Vancomycin	Vancomycin
Matrix	Serum or Plasma	Serum or Plasma
Calibration Form	Liquid	Liquid
Calibrator Levels	Two (2) Levels (0 and 50 µg/mL)	Six (6) Levels
Storage	2°C to 8°C until expiration date	2°C to 8°C until expiration date
Stability	Until expiration date noted on vial label and Package Insert for Kit and reconstituted reagents	Until expiration date noted on vial label.

J. Standard/Guidance Document Referenced (if applicable): NCCLS Protocol EP5-A

K. Test Principle:

The CEDIA® Vancomycin Assay uses recombinant DNA technology to produce a unique homogeneous enzyme immunoassay system. The assay is based on bacterial enzyme β -galactosidase, which has been genetically engineered into two inactive fragments i.e. enzyme acceptor (EA) and enzyme donor (ED). These fragments spontaneously reassociate to form fully active enzyme that, in the assay format, cleaves a substrate, generating a color change that can be measured spectrophotometrically.

In the assay, analyte in the sample competes with analyte conjugated to one inactive fragment of β -galactosidase for antibody binding site. If analyte is present in the sample, it binds to antibody, leaving the inactive enzyme fragments free to form active enzyme. If analyte is not present in the sample, antibody binds to analyte conjugated on the inactive fragment, inhibiting the reassociation of inactive β -galactosidase fragments, and no active enzyme is formed. The amount of active enzyme formed and resultant absorbance change are directly proportional to the amount of drug present in the sample.

L. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*

Inter-assay reproducibility (or within-run precision) was determined by assaying 6 replicates each of 3 commercially available controls in 20 separate runs giving a final sample size of 120 points for each control (per NCCLS protocol EP5-A) using the CEDIA Vancomycin Assay.

The results show that the intra-assay reproducibility for the 3 controls on both instruments were all <10% and comparable to values for the predicate device (K955851)

	<i>Bio Rad Control</i>		
	<i>Low</i>	<i>Medium</i>	<i>High</i>
<i>n</i>	<i>120</i>	<i>120</i>	<i>120</i>
<i>Avg (µg/mL)</i>	<i>6.03</i>	<i>18.97</i>	<i>32.41</i>
<i>SD (µg/mL)</i>	<i>0.4</i>	<i>0.64</i>	<i>0.85</i>
<i>CV %</i>	<i>6.7</i>	<i>3.4</i>	<i>2.6</i>

b. *Linearity/assay reportable range:*

The CEDIA Vancomycin Assay is designed to quantitate patient samples between 1.6µg/mL and 80µg/mL. Specimens with results greater than 80 µg/mL can be reported as > 80µg/mL or diluted with Vancomycin low Calibrator as appropriate and reassayed.

c. *Traceability (controls, calibrators, or method):*

High and low calibrators are prepared from a protein matrix containing bovine serum albumin and preservatives. The low calibrator contains no analyte, i.e. 0 µg/mL Vancomycin. The high calibrator is prepared by adding a stabilizer to the protein matrix containing 50 µg/mL Vancomycin. The calibrators are prepared in liquid form, and are sold as a set (2 x 7.5 mL, 2 x 5.0 mL). They may be used with any CEDIA® Vancomycin Assay reagent lot.

d. *Detection limit*

The sensitivity, or lowest detectable dose (LDD), is defined as the lowest concentration of analyte detectable when performing the assay according to the standard assay procedure. Sensitivity is established by determining the average concentration of analyte present for 21 replicates of the negative calibrator on each of two instruments. Once the average concentration is determined, sensitivity is calculated by adding 2 standard deviations to the average (or to zero if the average concentration is less than 0). Sensitivity or LDD for the DEDIA® Vancomycin Assay is 1.53µg.mL Vancomycin.

Sensitivity (Least Detectable Dose)

	Run 1 (µg/mL)	Run 2 (µg/mL)
n	21	21
Avg	-0.20	-0.16
SD	0.76	0.36
Sensitivity	1.53	0.73

e. Analytical specificity:

The potential cross-reactivity of endogenous physiologic substances on recovery of Vancomycin in the CEDIA® Vancomycin Assay was assessed by adding known amounts of potentially interfering endogenous substances to serum specimens having a known Vancomycin concentration. Two samples were devised, one with an approximate final concentration of 7 µg/mL Vancomycin/mL and the other with a final approximate concentration of 35 µg/mL. None of the endogenous substances tested at the supraphysiologic concentrations tested cross-reacts with reagents in the CEDIA® Vancomycin Assay producing a relative under- or over-recovery at either end of the assay range as indicated in the table below.

Interfering Substances – Cross Reactivity with Endogenous Substances

Interfering Substance	Final Concentration	Vancomycin (7 µg/mL)			Vancomycin (35 µg/mL)		
		Control Dose	Spike Dose	% of Control	Control Dose	Spike Dose	% of Control
Triglyceride	1000 mg/dL	9.3	9.2	99.1	33.6	34.1	101.4
Bilirubin	66 mg/dL	6.5	6.5	99.8	34.6	35.1	101.4
Γ-globulin	6 g/dL	9.2	8.5	92.7	34.4	33.9	98.5
Hemoglobin	1000 ng/dL	6.8	6.7	99.0	34.1	37.0	108.7
Albumin	4 g/dL	7.0	6.5	92.7	34.4	31.2	90.7
RF*	1800 IU/mL	9.5	9.3	97.8	35.9	35.5	99.1

*.RF = Rheumatoid Factor

f. Assay cut-off:

Not Applicable

2. Comparison studies:*a. Method comparison with predicate device:*

To demonstrate substantial equivalence between the CEDIA® Vancomycin and Abbott AxSYM® Vancomycin II Assays, 120 clinical serum specimens were obtained and assayed using the subject and predicate devices. The sample population included specimens with concentrations of Vancomycin across the dynamic range of the assay, 1.6 to 77.5 µg/mL. The relationship between Vancomycin concentrations derived using each device was evaluated

using conventional least squares regression, Deming's and least squares regression parameters, shows agreement between the CEDIA® Vancomycin Assay (y) and the AxSYM® Vancomycin II Assay (x) as demonstrated in the table below:

Method Comparison for Determination of Vancomycin Using the CEDIA® and AxSYM® Vancomycin II Assays

	Deming's	Least Squares
n	120	120
Equation	$y = 0.94x - 0.68$	$y = 0.93 - 0.42$
S.S.S	2.11	2.90
r	0.991	0.991

b. Matrix comparison:

The relationship between Vancomycin concentrations assayed using both the CEDIA® Vancomycin and Abbott AxSYM® Vancomycin II Assay was evaluated using linear regression techniques for 120 serum and 36 plasma specimens representing the dynamic range of the assay (from 1.6 to 77.5 µg Vancomycin/mL). The correlation coefficients as well as Deming and least squares regression parameters are indicated in the table below:

Regression CEDIA v. AxSYM (Serum)

	Deming's	Least Squares
n	120	120
Equation	$y = 0.94x - 0.68$	$y = 0.93 - 0.42$
S.S.S	2.11	2.90
r	0.991	0.991

Regression CEDIA v. AxSYM (Plasma)

	Deming's	Least Squares
n	36	36
Equation	$y = 0.92x - 0.67$	$y = 0.92 + 0.67$
S.S.S	1.20	1.64
r	0.994	0.994

3. Clinical studies:

a. Clinical sensitivity:

The minimum detectable concentration of the CEDIA Vancomycin Assay is 1.6 µg/mL

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type.

c. Other clinical supportive data (when a and b are not applicable):

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

In most adults a peak therapeutic response is achieved with Vancomycin concentrations between 20 – 40 µg/mL. Trough concentrations between 5 - 15 µg/mL usually ensure that drug elimination is adequate. Toxicity is correlated with very high levels (60 – 80 µg/mL) of Vancomycin. Various factors such as the general state of patient's health, severity of infection, time of sample collection, dosage, and dosage form, mode of drug administration, concomitant drug therapy and variations in individual drug absorption, distribution and excretion can potentially affect the serum Vancomycin concentration. These factors should be considered when interpreting the results.

Normal ranges were determined from literature!. Cook FV and Farrar WE: Vancomycin revisited. Ann Intern Med 88, 813 (1978).

M. Conclusion:

Based on the information provided in this submission, I recommend that the Microgenics CEDIA ® Vancomycin Assay is substantially equivalent to the currently marketed Abbott AxSYM ® Vancomycin II Assay (K955851)