

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

A. 510(k) Number:

k060709

B. Purpose for Submission:

Clearance of a new device

C. Measurand:

Gentamicin

D. Type of Test:

Turbidimetric Immunassay

E. Applicant:

Seradyn, Inc.

F. Proprietary and Established Names:

Multigent Gentamicin

G. Regulatory Information:

1. Regulation section:
21 CFR § 862.3450, Gentamicin test system.
2. Classification:
Class II
3. Product code:
LCD, enzyme immunoassay, gentamicin
4. Panel:
Toxicology (91)

H. Intended Use:

1. Intended use(s):
The Multigent Gentamicin assay is intended for the quantitative determination of Gentamicin in human serum or plasma on the Architect C8000 System.

The results obtained are used in the diagnosis and treatment of gentamicin overdose and in monitoring levels of gentamicin to help ensure appropriate therapy.

2. Indication(s) for use:
See Intended Use.

3. Special conditions for use statement(s):
For prescription use.
4. Special instrument requirements:
The ARCHITECT c8000 System.

I. Device Description:

The Multigent Gentamicin assay system is a homogeneous assay utilizing particle agglutination technology and is based on the competitive binding principle. The assay consists of reagents R1: anti-gentamicin monoclonal antibody and R2: gentamicin-coated microparticles. A six-level set of Multigent Gentamicin Calibrators (A through F) is used to calibrate the assay.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Abbott TDx/TDxFLx Gentamicin
2. Predicate 510(k) number(s):
k904226
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Intended for the quantitative determination of gentamicin in human serum or plasma.	A reagent system for the quantitative measurement of gentamicin, an antibiotic drug in human serum or plasma.
Calibration	Six levels	Six levels
Sample Types	Plasma and Serum	Plasma and Serum

Differences		
Item	Device	Predicate
Methodology	Homogeneous particle-enhanced turbidimetric immunoassay (particle agglutination).	Florescence Polarization Immunoassay (FPIA) technology.
Instrument Required	Abbott ARCHITECT c8000 System.	Abbott TDx/TDxFLx

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

CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods

CLSI EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach

CLSI EP9-A2, Evaluation of Precision Performance of Quantitative Measurement Methods

L. Test Principle:

In particle agglutination assays, the degree of agglutination is inversely proportional to the quantity of free drug in the reaction cell. If no drug is present in the sample, the antibodies in the Multigent Gentamicin Antibody Reagent (R1) will bind only to the bound drug on the particle which will cause it to agglutinate and will result in higher absorbance. If increased amount of competing drug is present in the sample, this will result in decreased binding of bound drug by the antibody, resulting in a relative decrease in particle agglutination, which will result in lower absorbance. Therefore, the absorbance is inversely proportional to the concentration of drug.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Three control levels (Low Control, Mid Control, and High Control) were evaluated on the ARCHITECT c8000 and, after 2 hours within the same day, the samples were re-run in duplicate, over 20 days resulting in a total of 80 replicates for each control. Calibration was performed initially and re-calibration was performed when the controls did not recover within labeled ranges. Results for precision are summarized below.

Precision on the ARCHITECT c8000

	Low Control	Mid Control	High Control
N	80	80	80
Mean, $\mu\text{IU/mL}$	2.68	6.47	9.41
	SD (%CV)	SD (%CV)	SD (%CV)
Within Run	0.08(2.93)	0.07(1.09)	0.14(1.53)
Between Run	0.06(2.17)	0.07(1.07)	0.07(0.70)
Between Day	0.12(4.37)	0.12(1.91)	0.13(1.34)
Total	0.15(5.69)	0.16(2.44)	0.20(2.15)

- b. *Linearity/assay reportable range:*

The reportable range of the assay is 0.34 – 10.0 $\mu\text{g/mL}$ (highest calibrator).

The sponsor evaluated the recovery of samples across most of the measuring range. Two groups of samples were used ranging from 1.72 to 6.88 $\mu\text{g/mL}$ and 0.25 to 8.00 $\mu\text{g/mL}$. Samples were prepared by spiking and dilution. The

samples were run in triplicate. The percent recovery for each sample was determined by dividing the mean observed result by the theoretical value. Results are summarized below.

	Theoretical Conc. (µg/mL)	Rep 1	Rep 2	Rep 3	Mean Recovered Conc.	SD	%CV	% Recovery
Study 1	6.88	7.14	7.31	7.14	7.20	0.098	1.36	104.60%
	5.16	5.20	5.23	5.39	5.27	0.102	1.94	102.20%
	3.44	3.50	3.65	3.70	3.62	0.104	2.88	105.14%
	1.72	1.59	1.67	1.66	1.64	0.044	2.66	95.35%
	Mean Percent Recovery							101.82%
Study 2	0.25	0.23	0.28	0.26	0.26	0.025	9.82	102.67%
	1.00	1.02	0.99	0.98	1.00	0.021	2.09	99.67%
	2.25	2.24	2.22	2.21	2.22	0.015	0.69	98.81%
	4.50	4.44	4.55	4.42	4.47	0.070	1.57	99.33%
	8.00	8.12	7.99	8.15	8.09	0.085	1.05	101.08%
	Mean Percent Recovery							100.31%

Linear regression analysis gave the following:

Study 1: Observed = 1.0657(Expected) – 0.15; r = 0.9989

Study 2: Observed = 1.01(Expected) – 0.024; r = 0.9999

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The Multigent Gentamicin Calibrators the assay utilizes are currently marketed and were cleared under k981706. Calibration is stable for 28 days for this assay.

d. Detection limit:

The Limit of Quantitation (LoQ) (defined by the sponsor as the analytical concentration at which the precision of the assay [%CV] is less than 20% and the accuracy is within 10%) was determined by diluting a patient sample with known concentration gentamicin with human serum (negative for gentamicin) to achieve an approximate concentration of 0.5 µg/mL. This sample was further diluted with negative serum to achieve approximate gentamicin concentrations of 0.4, 0.3, 0.2, and 0.1 µg/mL. All samples were then run on an ARCHITECT c8000 System. The data submitted supports a LoQ of 0.33 µg/mL. The sponsor will claim a higher LoQ of 0.34 mg/dL in the labeling. Results of this study are summarized below.

N	20	20	20	20	20	20
Mean, μIU/mL	0.00	0.10	0.20	0.30	0.40	0.50
	SD (%CV)	SD (%CV)	SD (%CV)	SD (%CV)	SD (%CV)	SD (%CV)
Total	0.025(56.04)	0.039(30.26)	0.027(10.94)	0.050(14.89)	0.034(7.89)	0.038(7.37)

The Least Detectable Dose (LDD) or analytical sensitivity (the lowest amount of analyte in a sample that can be distinguished from zero with 95% confidence) was determined. The sponsor claims a LDD of 0.1 μg/mL.

e. Analytical specificity:

Serum samples with gentamicin stock concentrations of 2.46 and 3.44 μg/mL were spiked with bilirubin (20 mg/dL), hemoglobin (2000 mg/dL), triglyceride (1691 mg/dL), total protein (12 g/dL), and Rheumatoid Factor (582 IU) and run in triplicate (hemoglobin in duplicate). The endogenous substances above were found not to interfere within the sponsor's percent recovery acceptance criteria of 100±10%. HAMA Type-1 and Type-2 samples were also spiked with 3.33 μg/mL gentamicin. HAMA Type-1 and Type-2 were found not to interfere (percent recovery within 100±10%).

For the Common Co-Administered Drugs study, two amounts of gentamicin were present in the samples used: 1.5μg/mL and 3.5μg/mL. The following nine test samples had 1.5μg/mL of gentamicin present during testing with a range of 1.55μg/mL to 1.59μg/mL: Theophylline, Cyclosporin, Rifampicin, Acetaminophen, Ibuprofen, Penicillin V, Phenylbutazone, Acetylsalicylic acid and Metronidazole. All other samples had 3.5μg/mL of gentamicin present during testing with a range of 3.51μg/mL to 3.88μg/mL. The interference results are listed in the package insert.

Cross-reactivity of 50.35% was observed for sisomicin.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Sixty-eight purchased clinical samples were tested (ranging from 0.22 μg/mL to 9.97 μg/mL). A Passing-Bablok regression analysis was performed comparing device results to predicate results. Results of the analysis gave the following linear regression statistics:

$$\text{Device} = 1.122(\text{Predicate}) - 0.445; r = 0.996$$

b. Matrix comparison:

A study was conducted to determine the performance of the assay for both serum and plasma samples containing gentamicin.

Blood was drawn from ten healthy donors (with no gentamicin therapy) for each tube type listed below:

- Plastic K2 EDTA tube
- Glass K3 EDTA tube
- Glass plasma separator lithium heparin tube
- Glass sodium heparin tube
- Glass lithium heparin tube
- Glass serum separator tube
- Plastic tube with clot activator
- Glass tube with no additives
- Plastic tube with no additives.

The serum or plasma was removed from the collection tubes and aliquoted into new tubes for testing (which is the same procedure the customer would use). Serum or plasma from each tube was then spiked with gentamicin. The samples were analyzed on the ARCHITECT c8000 analyzer in duplicate with baseline results obtained on day zero for each type of tube. Results support that the collection tubes evaluated show no adverse effects on gentamicin (recovery within 100 +/- 10%).

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

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

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The sponsor cites a therapeutic range for gentamicin for moderate infections as 2 – 8 µg/mL. Peak serum levels of 5 -10 µg/mL have been shown to cause renal

and CNS toxicity. Recommended trough levels are < 2 µg/mL to avoid associated nephrotoxicity.

The reference ranges are referenced from:

Tietz N. *Clinical Guide to Laboratory Tests*. 2nd ed. Philadelphia, PA: WB Saunders; 1990;742.

Nordstrom L, Banck G, Belfrage S, et al. Prospective study of the ototoxicity of gentamicin. *Acta Pathol Microbiol Immunol Scand (B)* (Supp 241) 1973;58-61.

Dayal VS, Smith EL, McCain WG. Cochlear and vestibular gentamicin toxicity. A clinical study of systemic and topical usage. *Arch Otolaryngol* 1974;100:338-40

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.