

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

A. 510(k) Number:

k052815

B. Purpose for Submission:

New device

C. Measurand:

Amikacin

D. Type of Test:

Quantitative, Immunoturbidimetric assay

E. Applicant:

Seradyn, Inc.

F. Proprietary and Established Names:

QMS® Amikacin Reagents

G. Regulatory Information:

1. Regulation section:

21 CFR §862.3035; Amikacin Test System

2. Classification:

Class II

3. Product code:

KLQ

4. Panel:

91, Toxicology

H. Intended Use:

1. Intended use(s):

See Indications for use below

2. Indication(s) for use:

The QMS® Amikacin assay is intended for the quantitative determination of amikacin in human serum or plasma on automated clinical chemistry analyzers.

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

3. Special conditions for use statement(s):

For Prescription use only.

4. Special instrument requirements:

This device was used on the Roche Hitachi 717 Analyzer (k872494).

I. Device Description:

The QMS® Amikacin assay consists of separately packaged reagents (R1 and R2) and calibrators. R1 is the antibody reagent that contains anti-Amikacin monoclonal antibody (mouse ascites) in a buffer with sodium azide as a preservative. R2 is Amikacin micro-reagent that contains Amikacin coated microparticles in buffer containing stabilizers and sodium azide as a preservative. Both reagents are supplied in liquid form. The calibrators that are provided with the assay were previously cleared in k903101 as the Innofluor Amikacin Calibrator Set. The calibrators consist of six levels of one mL liquid form.

The human serum used for the already cleared calibrators were tested by FDA approved methods and confirmed to be non-reactive for Hepatitis B surface Ag (HBsAg), HIV Type 1 and 2 antibodies and Hepatitis C antibodies.

J. Substantial Equivalence Information:

1. Predicate device name(s):

TDx/TDxFLx Amikacin Assay

2. Predicate 510(k) number(s):

k802669

3. Comparison with predicate:

| Similarities | | |
|---------------------|---|------------------|
| Item | Device | Predicate |
| Indications for Use | The results obtained are used in the diagnosis and treatment of amikacin overdose and in monitoring levels of amikacin to ensure appropriate therapy. | same |
| Calibration | Six levels | same |
| Matrix | Serum and plasma | same |

| Differences | | |
|--------------------|---|---|
| Item | Device | Predicate |
| Methodology | Homogeneous particle-enhanced turbidimetric immunoassay (particle agglutination) | Fluorescence Polarization Immunoassay (FPIA) technology. |
| Reagent component | Two reagent system –R1 anti-amikacin antibody (mouse) reagent and R2 amikacin-coated Microparticle reagent. | Three reagent system – pretreatment solution, S Amikacin antiserum (sheep) and T Amikacin Fluorescein Tracer. |

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

The sponsor reference the following guidance document(s) in their submission:

CLSI document EP6-P; Evaluation of the Linearity of Quantitative Measurement.

CLSI document EP9-A; Method Comparison and Bias Estimation Using Patient Samples.

CLSI document EP5-A. Method Comparison of Precision Performance of Clinical Chemistry Devices; Approved Guideline

CLSI document EP7-P. Interference Testing in Clinical Chemistry.

L. Test Principle:

The QMS Amikacin assay is a homogeneous particle-enhanced turbidimetric immunoassay. The assay is based on competition between drug in the sample and drug coated onto a microparticle for antibody binding sites of the amikacin antibody reagent. The amikacin-coated microparticle reagent is rapidly agglutinated in the presence of the anti-amikacin antibody reagent and in the absence of any competing drug in the sample. The rate of absorbance change is measured photometrically. When a sample containing amikacin is added, the agglutination reaction is partially inhibited, slowing down the rate of absorbance change. A concentration-dependent classic agglutination inhibition curve can be obtained with maximum rate agglutination at the lowest amikacin concentration and the lowest agglutination rate at the highest amikacin concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision was determined as described in CLSI protocol EP5. Precision was run on the Hitatch 717, using QMS Amikacin Calibrators and commercially available controls. Each sample was run in duplicate for 20 non-consecutive days. Additionally, within run precision was conducted by re-running the samples again after two hours. The acceptance criterion was a total CV of <10%. The results are shown in the tables below:

| | | | Within Run | | Between Run | | Total | |
|--------------|----|---------------|------------|------|-------------|------|-------|------|
| | N | Mean µg/mL | SD | CV % | SD | CV% | SD | CV% |
| Low Control | 80 | 4.09 | 0.22 | 5.37 | 0.19 | 4.77 | 0.41 | 9.94 |
| Mid Control | 80 | 12.00 | 0.21 | 1.79 | 0.08 | 0.70 | 0.74 | 6.22 |
| High Control | 80 | 24.37 | 0.47 | 1.93 | 0.40 | 1.65 | 1.54 | 6.32 |

Commercially available control levels

| Controls | Amikacin (µg/mL) |
|----------|------------------|
| Level 1 | 5.1 (4.1-6.2) |
| Level 2 | 14 (11-17) |
| Level 3 | 29 (23-34) |

Accuracy by Recovery was determined by spiking human serum that was negative for amikacin with USP traceable amikacin to achieve concentrations of 18.4 and 9.2 µg/mL. The samples were analyzed in duplicate with the QMS Amikacin assay. Acceptance criterion is 100 ± 10 % recovery. The overall recovery was 94.02%.

b. Linearity/assay reportable range:

Linearity was conducted and assessed according to CLSI EP6. The sponsor claims the reportable range of the assay is 1.5 µg/mL to 50 µg/mL. Each level of calibrator was diluted with equal volumes of the next higher level calibrator to obtain mid-point concentrations (µg/mL) of 1.5, 6.5, 15.0, 27.5 and 42.5. Samples were run in duplicate and the mean recovered concentration used.

| Theoretical Conc. µg/mL | Mean Recovered Conc. | SD | CV% | % Recovery |
|-------------------------|----------------------|------|------|------------|
| 1.5 | 1.67 | 0.10 | 5.99 | 111.33 |
| 6.5 | 6.48 | 0.04 | 0.54 | 99.69 |
| 15.0 | 14.67 | 0.18 | 1.19 | 97.80 |
| 27.5 | 26.32 | 0.37 | 1.41 | 95.71 |
| 42.5 | 41.44 | 0.20 | 0.47 | 97.51 |
| Mean Percent Recovery | | | | 100.41 |

A linear regression analysis plot of USP Amikacin against recovered amikacin resulted in a line with a correlation coefficient (R^2) of 0.9998, demonstrating that the assay is linear.

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

The QMS Amikacin assay does not include amikacin controls or calibrators. Calibrators were cleared under k903101. The controls used with this assay are commercially available.

d. Detection limit:

The analytical sensitivity, or lowest detectable dose (LLD), is defined as the concentration at which the lowest concentration is distinguishable from zero with 95% confidence. Sensitivity was established by determining the average concentration of analyte present in 21 replicated of the zero calibrator. The analytical sensitivity for this assay was determined to be 0.54 µg/mL which supports the sponsors claim of 0.8 µg/mL.

e. *Analytical specificity:*

Interference testing was conducted in duplicate or triplicate using the QMS Amikacin assay. For the following interfering substances at the concentration listed, the QMS Amikacin assay showed less than a 10% error in detecting amikacin.

| Interfering Substances | Interferent Concentration | N | Amikacin (µg/mL) | % Recovery |
|------------------------|---------------------------|---|------------------|------------|
| Bilirubin | 15 mg/dL | 2 | 21.65 | 96.40 |
| Hemoglobin | 10 g/L | 2 | 17.32 | 93.42 |
| Triglyceride | 1691 mg/dL | 3 | 24.03 | 96.30 |
| Total Protein | 12 g/L | 3 | 24.03 | 96.00 |
| HAMA Type-1 | Normal human level | 2 | 20.31 | 100.5 |
| HAMA Type-2 | Normal human level | 2 | 17.32 | 98.04 |

The following compounds were tested for cross-reactivity

| Cross-reactant Drug | Conc. Test µg/mL | Percent Cross-Reactivity |
|---------------------|------------------|--------------------------|
| 5-Fluorocytosine | 30 | -0.39 |
| Amphotericin | 100 | 1.33 |
| Ampicillin | 50 | ND |
| Carbenicillin | 2500 | ND |
| Cephalexin | 320 | ND |
| Cephalosporin C | 1000 | ND |
| Cephalothin | 1000 | ND |
| Chloramphenicol | 250 | 0.55 |
| Clindamycin | 2000 | ND |
| Erythromycin | 500 | ND |
| Ethacrynic acid | 400 | ND |
| Furosemide | 100 | 1.00 |
| Fusidic acid | 1000 | ND |
| Gentamicin | 100 | ND |
| Kanamycin A | 400 | ND |
| Kanamycin B | 400 | ND |
| Lincomycin | 2000 | ND |
| Methicillin | 200 | 0.41 |
| Methotrexate | 500 | ND |
| Methylprednisolone | 200 | 0.638 |
| Neomycin | 1000 | ND |
| Netilmycin | 125 | ND |

| Cross-reactant Drug | Conc. Test µg/mL | Percent Cross-Reactivity |
|---------------------|------------------|--------------------------|
| Oxytetracycline | 2000 | ND |
| Penicillin V | 100 | 1.38 |
| Prednisolone | 12 | 2.36 |
| Rifampicin | 500 | ND |
| Spectinomycin | 100 | ND |
| Streptomycin | 400 | ND |
| Sulfadiazine | 1000 | ND |
| Sulfamethoxazole | 400 | ND |
| Tetracycline | 2000 | ND |
| Tobramycin | 100 | 0.32 |
| Trimethoprim | 200 | ND |
| Vancomycin | 400 | ND |

*ND – Non Detected

f. Assay cut-off:

See detection limit section above.

2. Comparison studies:

a. Method comparison with predicate device:

Fifty-six serum and plasma samples were tested and compared to the predicate method. Samples ranged from 2.38 to 37.58 µg/mL. Passing-Bablok regression analysis yielded an equation of $y=1.00x + 0.245$ (95% confidence intervals of the slope and intercept were 0.977 to 1.022 and -0.049 to 0.544, respectively). The correlation coefficient of the paired data was $r = 0.992$

b. Matrix comparison:

The sponsor demonstrated equivalence between serum and plasma by conducting the following studies: performance characteristics of the assay for serum and plasma studies and interferences when using different types of collection tubes and stability at 2 to 8 °C and <-10 °C storage conditions.

Blood was drawn from 10 healthy donors (no amikacin therapy) for each of the following tube types; plastic K2 and K3 EDTA, glass plasma separator lithium heparin, glass sodium heparin, glass lithium heparin, glass serum separator, plastic tube with clot activator, glass tube no additive (served as the control) and plastic tube no additive. Amikacin was spiked into each of the samples which were then run in duplicate and the resulted were averaged to obtain a mean. The results as shown in the table below indicate no significant differences between the recovery of amikacin in serum or plasma. The collection tubes evaluated showed no adverse effects on the amikacin recovery and support the claim for both serum and plasma samples with the

QMS Amikacin assay.

| Donor | | Tube Type | | | | | | | | |
|------------------|------------|-----------------------------|---------------------------------|-------------------------------|----------------------------|--------------------|-----------------------------|-------------------|------------|------------|
| | | Serum – glass Control | Serum- plastic w/silicone | Serum w/clot activators | Serum separator tube | Lithium heparin | Plasma separator tube | Sodium heparin | K3 EDTA | K2 EDTA |
| A | Mean | 19.49 | 20.11 | 18.93 | 19.45 | 20.21 | 19.80 | 19.78 | 18.78 | 20.60 |
| | % recovery | 100 | 103.21 | 97.13 | 99.82 | 103.72 | 101.62 | 101.51 | 96.38 | 105.7 |
| B | Mean | 20.37 | 19.99 | 19.83 | 19.52 | 21.48 | 19.95 | 20.22 | 19.67 | 20.60 |
| | % recovery | 100 | 98.13 | 97.37 | 95.83 | 105.48 | 97.94 | 99.26 | 96.56 | 101.2 |
| C | Mean | 19.61 | 20.03 | 20.30 | 19.76 | 20.47 | 21.80 | 19.90 | 19.96 | 21.15 |
| | % recovery | 100 | 102.14 | 103.52 | 100.77 | 104.39 | 111.17 | 101.48 | 101.8 | 107.9 |
| D | Mean | 20.30 | 20.37 | 19.73 | 19.49 | 20.91 | 22.79 | 19.62 | 21.28 | 19.40 |
| | % recovery | 100 | 100.32 | 97.19 | 95.99 | 103 | 112.24 | 96.65 | 104.8 | 95.57 |
| E | Mean | 20.32 | 20.12 | 20.09 | 19.57 | 20.64 | 19.41 | 19.77 | 20.48 | 21.27 |
| | % recovery | 100 | 99.02 | 98.84 | 96.31 | 101.55 | 95.52 | 97.27 | 100.8 | 104.7 |
| F | Mean | 21.13 | 20.07 | 19.54 | 19.10 | 20.66 | 18.69 | 20.26 | 20.79 | 20.45 |
| | % recovery | 100 | 94.98 | 92.45 | 90.37 | 97.78 | 88.45 | 95.86 | 98.39 | 96.76 |
| G | Mean | 21.26 | 19.74 | 20.57 | 19.63 | 21.87 | 19.79 | 19.81 | 20.28 | 21.02 |
| | % recovery | 100 | 92.87 | 96.78 | 92.33 | 102.87 | 93.11 | 93.20 | 95.39 | 98.89 |
| H | Mean | 20.90 | 19.20 | 22.71 | 19.72 | 20.88 | 19.58 | 19.43 | 20.64 | 21.24 |
| | % recovery | 100 | 91.84 | 108.66 | 94.35 | 99.90 | 93.66 | 92.97 | 98.76 | 101.6 |
| I | Mean | 20.94 | 19.44 | 22.41 | 18.87 | 20.72 | 19.66 | 20.05 | 22.13 | 19.39 |
| | % recovery | 100 | 92.86 | 107.05 | 90.11 | 98.97 | 93.91 | 95.77 | 105.7 | 92.60 |
| J | Mean | 20.47 | 19.62 | 23.98 | 19.74 | 20.46 | 19.68 | 19.38 | 21.92 | 19.34 |
| | % recovery | 100 | 95.87 | 117.18 | 96.43 | 99.98 | 96.16 | 94.70 | 107.1 | 94.50 |
| Grand Mean | | 20.48 | 19.87 | 20.81 | 19.48 | 20.83 | 20.11 | 19.82 | 20.59 | 20.44 |
| Grand % recovery | | 100 | 97.03 | 101.62 | 95.14 | 101.72 | 98.23 | 96.80 | 100.6 | 99.84 |

The sample from all tube types were divided into two portions and stored at 2-8 °C and <-10 °C. Sample stability for 2-8 °C was run on days 3, 7 and 14 while the stability studies for <-10 °C were run on days 7, 14 and 30. The results showed that there were no interferences with regard to recovery of amikacin in serum or plasma for the 9 tube types tested. The results also showed that the samples are stable at 2-8 °C for 7 days and 14 days at <-10 °C.

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):

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Therapeutic peak serum values of 20 to 25 µg/mL and trough level of 5 to 10 µg/mL are generally accepted for therapeutic effectiveness. The most serious toxic effect is permanent damage to the vestibular division of the eighth cranial nerve, which has been reported to occur most frequently in patients with renal failure. Toxicity is associated with peak levels greater than 35 µg/mL and trough values greater than 10 µg/mL. Each laboratory should investigate the transferability of the expected values to its own patient population and, if necessary, determine its own reference range.

Sponsor reference literature for these expected values/reference ranges. Zaska DE et al: Amikacin/kanamycin: Therapeutic use and serum concentration monitoring, in Taylor WJ and Finn AL (eds): Individualizing Drug Therapy: Practical Applications of Drug Monitoring. New York, Gross, Townsend, Frank, Inc, 1981: vol 1, pp 67-111.

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.