

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

A. 510(k) Number:

K033884

B. Reason for Submission:

New Product

C. Analyte:

Amikacin

D. Type of Test:

Quantitative immunoturbidimetric assay

E. Applicant:

Radox Laboratories LTD

F. Proprietary and Established Names:

Radox Amikacin

G. Regulatory Information:

1. Regulation section:
21CFR §862.3035 -Amikacin test system.
2. Classification:
Class 2
3. Product Code:
KLP
4. Panel:
Toxicology (91)

H. Intended Use:

1. Intended use(s):
This test is for the quantitative *in vitro* determination of amikacin in human serum on automated clinical chemistry analyzers.
2. Indication(s) for use:
Measurements obtained by this device are used in the diagnosis and treatment of amikacin use or overdose and in monitoring levels of amikacin to ensure appropriate therapy.
3. Special condition for use statement(s):
None
4. Special instrument Requirements:
Advia 1650 analyzer

I. Device Description:

The device/test is composed of two liquid components: anti-amikacin antibody (mouse origin) in buffer and a latex particle containing solution.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Behring Diagnostics EMIT Amikacin Test Kit
2. Predicate K number(s):
K840193
3. Comparison with predicate:
The assays have in common: intended use, matrix, and linear range. The assays differ in the details of their methodology: the predicate is an enzyme-based immunoassay that correlates amikacin concentration with a change in light absorbance at 340 nm while the Randox assay is an immunoturbidimetric assay that correlates amikacin concentration with a change in scattered light intensity.

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

The sponsor states that imprecision estimates were determined by the method in NCCLS EP5-A.

L. Test Principle:

The assay is a latex-enhanced immunoturbidimetric assay that is based on measuring changes in scattered light. The latex particles are coated with amikacin, which rapidly agglutinates in the presence of amikacin-specific antibody. If a sample containing amikacin is introduced, the agglutination reaction is inhibited in proportion to the concentration of amikacin present in the sample.

M. Performance Characteristics (if/when applicable):

All performance characteristics were established on an ADVIA 1650 analyzer in a Randox laboratory unless otherwise noted.

1. Analytical performance:
 - a. *Precision/Reproducibility*
Precision was determined by assaying assay control material in duplicate for 11 days, 2 runs per day. According to the sponsor, calculations were according to NCCLS EP5-A.

Randox Amikacin Assay Precision

| Concentration (n) | Mean-ng/mL | Within-run precision | | Total precision | |
|----------------------|------------|----------------------|-----|--------------------|-----|
| | | standard deviation | %CV | standard deviation | %CV |
| Control Level 1 (43) | 37.9 | 0.017 | 4.5 | 0.21 | 5.5 |
| Control Level 2 (44) | 146.9 | 0.27 | 1.9 | 0.47 | 3.2 |
| Control Level 3 (44) | 295.4 | 0.35 | 1.2 | 0.7 | 2.4 |

- b. *Linearity/assay reportable range*

The sponsor claims the reportable range of the assay is 0.13 ug/mL to the level of the highest calibrator (~50 ug/mL). They determined this by diluting the highest calibrator to 80%, 60%, 40%, and 20% of the original value and read 3 times. Using a linear fit based on the 20%, 40%, and 60% levels, which roughly correspond to the therapeutic range (see below) the parameters are: slope 0.999, and r value 0.998. The lower limit claim is based on the detection level (see below). It was not tested in these linearity studies.

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

Not applicable.

d. *Detection limit:*

The sponsor reports that the sensitivity of the assay is 0.13 ug/mL. This value was the mean of a zero sample assayed 45 times plus 3 standard deviations.

e. *Analytical specificity:*

Bilirubin (25 mg/dL), hemoglobin (500 mg/dL), and triglyceride (500 mg/dL) were added to quinidine-spiked serum samples and did not interfere with quinidine recovery.

Compounds whose chemical structure or concurrent usage might interfere with amikacin recovery were added to normal serum at ten times the highest concentration for its therapeutic range:

Specificity of Randox Amikacin Assay

| Compound Tested | Concentration Tested (ug/mL) | Cross-reactivity (%) |
|-----------------|------------------------------|----------------------|
| Gentamycin | 100 | -0.86 |
| Kanamycin | 25 | -1.24 |
| Netilmicin | 80 | -0.83 |
| Streptomycin | 200 | -0.57 |
| Tobramycin | 100 | -0.91 |

f. *Assay cut-off:*

See above.

2. Comparison studies:

a. *Method comparison with predicate device:*

Fifty serum samples were tested in duplicate, and compared to the predicate method, also tested in duplicate. Some of the samples were patient serum samples; others were normal serum spiked with concentrations of amikacin. Samples ranged in value from 0.85 ug/mL to 55.8 ug/mL. Regression analysis of the data yielded these parameters:

| | |
|-------------------|-------|
| Constant | -0.46 |
| Std Err of Y est. | 1.65 |
| R squared | 0.99 |

| | |
|----------------|------|
| n observations | 50 |
| Slope | 1.10 |

These values were within Randox's acceptance criteria. However, there was substantial variability and departure from the predicate in the samples above the therapeutic range (i.e. >30 ug/mL where the therapeutic range is 20 – 30 ug/mL) (r value 0.79, slope 1.11) so the manufacturer was asked to caution users to dilute and retest samples above 30 ug/mL.

b. Matrix comparison:

N/A

3. Clinical studies:

a. Clinical sensitivity:

N/A

b. Clinical specificity:

N/A

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

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

After an intramuscular injection of 500 mg of amikacin every 12 hours (15 mg/kg/d) peak drug levels in serum are 10-30 ug/mL. The target peak serum concentrations for an every-12-hours dosing regimen are 20-40 ug/mL (Chambers, H., "Aminoglycosides and Spectinomycin", Basic and Clinical Pharmacology – 9th Edition (2004)). However, effective treatment of serious infections may require serum concentrations outside these ranges. Therefore, this expected range serves only as a guideline.

N. Conclusion:

The submitted information in this pre-market notification is complete and supports a substantial equivalence decision.