QMS® Amikacin (AMIK)

thermo scientific

IVD **For In Vitro Diagnostic Use Only**

Rx Only

REF **0373910**

This Quantitative Microsphere System (QMS) package insert must be read carefully prior to use. Package insert instructions must be followed accordingly. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Intended 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 help ensure appropriate therapy.

Summary and Explanation of the Test

Amikacin is a semi-synthetic aminoglycoside that exhibits bactericidal activity against a wide range of pathogens, including many organisms resistant to other aminoglycosides.[1-4] Amikacin is active in vitro against gram-negative organisms, penicillinase and non-penicillinase producing staphylococci. The strength of this drug is due primarily to its high degree of resistance to aminoglycoside-inactivating enzymes.[5] Determination of serum or plasma drug levels is required to achieve optimum therapeutic efficacy and minimize toxicity.[6-7]

Principles of the Procedure

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 of agglutination at the lowest amikacin concentration and the lowest agglutination rate at the highest amikacin concentration.

Reagents

QMS Amikacin, **REF** 0373910, is supplied as a liquid, ready-to-use, two-reagent kit that contains:

REF 0373910

R1	Reagent 1	2 x 19 mL
R2	Reagent 2	2 x 7 mL

Reactive Ingredients

INGRED	Ingredient	Concentration
R1	Anti-amikacin Monoclonal Antibody (Mouse)	<1.0%
	Sodium Azide	≤0.1%
R2	Amikacin-coated Microparticles	≤0.5%
	Sodium Azide	≤0.1%

Reagent Handling and Storage

- **R1** and **R2** Ready for Use.
- Before use, invert several times, avoiding the formation of bubbles.
- Remove air bubbles, if present in the reagent cartridge, with a new applicator stick. Alternatively, allow the reagent to sit at the appropriate storage temperature to allow the bubbles to dissipate. To minimize volume depletion, do not use a transfer pipette to remove the bubbles.
- When either the **R1** or the **R2** reagent cartridge becomes empty, replace both cartridges and verify calibration with at least two levels of controls according to the established Quality Control requirements for your laboratory. If control results fall outside acceptable ranges, recalibration may be necessary.
- In the case of accidental spill, clean and dispose of material according to your laboratory's SOP, local, state, and country regulations, with consideration that the material contains potentially infectious materials.
- In the case of damaged packaging on arrival, contact your technical support representative (contact details listed at the end of this package insert).

⚠ **CAUTION:** Reagent bubbles may interfere with proper detection of reagent level in the cartridge, causing insufficient reagent aspiration that could impact results.

2°C–8°C The unopened reagents are stable until the expiration date when stored at 2 to 8°C. **Do not freeze reagents or expose them to temperatures above 32°C.**

Warnings and Precautions

Precautions for Users

- For in vitro diagnostic use.
- Do not mix materials from different kit lot numbers.
- Contains nonsterile mouse monoclonal antibodies.

DANGER: QMS Amikacin (AMIK) assay contains ≤3.5% Goat Serum, ≤1.0% Filtered mouse ascites fluid, and ≤3.0% Human Serum Albumin (HSA).
H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled.
H317 - May cause allergic skin reaction.

Avoid breathing mist or vapor. Contaminated work clothing should not be allowed out of the workplace. Wear protective gloves/eye protection/face protection. In case of inadequate ventilation wear respiratory protection. If on skin: Wash with plenty of soap and water. IF INHALED: If breathing is difficult, remove victim to fresh air and keep at rest in a position comfortable for breathing. If skin irritation or rash occurs: Get medical advice/attention. If experiencing respiratory symptoms: Call a POISON CENTER or doctor/physician. Wash contaminated clothing before reuse. Dispose of contents/container to location in accordance with local/regional/national/international regulations.

⚠ **CAUTION:** This product contains human sourced and/or potentially infectious components. Components sourced from human blood have been tested and found to be nonreactive for HBsAg, anti-HIV 1/2, and anti-HCV. No known test method can offer complete assurance that products derived from human sources or inactivated microorganisms will not transmit infection. Therefore, it is recommended that all human sourced materials be considered potentially infectious and handled with appropriate biosafety practices.

Specimen Collection and Handling

The following specimen collection tubes may be used for the QMS Amikacin assay:

	Glass	Plastic
Serum	• No Additive • Serum Separator Tube (gel) • Clot Activator	• Serum Separator Tube (gel)

Other specimen collection tubes have not been validated for use with the QMS Amikacin assay. Follow the manufacturer's processing instructions for serum or plasma tubes.

	Glass	Plastic
Plasma	• EDTA (K_3)	• EDTA (K_2) • Lithium Heparin • Sodium Heparin • Plasma Separator Tube with Lithium Heparin (gel)

Other specimen collection tubes have not been validated for use with the QMS Amikacin assay. Follow the manufacturer's processing instructions for serum or plasma tubes.

- Inadequate centrifugation of the specimen may cause an erroneous result.
- Ensure specimens are free of fibrin, red blood cells, and other particulate matter.
- Remove the plasma or serum from the cells, clot, or gel as soon as possible after collection. Some gel separator tubes may not be suitable for use with therapeutic drug monitoring assays; refer to information provided by the tube manufacturer.[8]
- Specimens removed from the cells, clot, or gel may be stored up to one week at 2 to 8°C. If testing will be delayed more than one week, specimens should be stored frozen (≤-10°C). Specimens frozen up to two weeks showed no performance differences from fresh samples. Care should be taken to limit the number of freeze-thaw cycles.

Procedure

Materials Provided

- QMS Amikacin Reagents, **REF** 0373910

Materials Required but not Provided

- QMS Amikacin Calibrators, **REF** 0374157
  CAL A-F: 1 x 1.0 mL each
- Amikacin Controls

Assay Procedure

For a detailed description of how to run and calibrate an assay, refer to the instrument specific operations manual.

Specimen Dilution Procedure

Use QMS Amikacin CAL A (0.0 µg/mL) to manually dilute samples outside the linearity of the assay.

Manual Dilution Protocol
A manual dilution can be performed on patient samples with amikacin concentrations reported as greater than 50.0 µg/mL by making a dilution of the specimen with QMS Amikacin CAL A (0.0 µg/mL) before pipetting the sample into the sample cup. The dilution must be performed so the diluted test results read greater than the assay technical sensitivity of 1.5 µg/mL. The concentration reported must be multiplied by the manual dilution factor to obtain the final sample concentration.

Final Sample Concentration = Reported Concentration x Manual Dilution Factor

$$\text{Manual Dilution Factor} = \frac{\text{Volume of Sample + Volume of CAL A)}}{\text{Volume of Sample}}$$

Calibration
The QMS Amikacin assay must be calibrated using a full calibration (6-point) procedure. To perform a full calibration, test the QMS Amikacin Calibrators A, B, C, D, E, and F in duplicate.

Calibration is required with each new lot number. Verify the calibration curve with at least two levels of controls according to the established Quality Control requirements for your laboratory. If control results fall outside acceptable ranges, recalibration may be necessary.

Note: Amikacin CAL A is the calibration blank for this assay.

Quality Control
As appropriate, refer to your laboratory Standard Operating Procedure(s) and/or Quality Assurance Plan for additional quality control requirements and potential corrective actions. All quality control requirements should be performed in conformance with local, state, and/or federal guidelines or accreditation requirements.

Recommended control requirements for the QMS Amikacin assay:

- A minimum of two levels of controls spanning the medical decision range should be run every 24 hours.
- If more frequent control monitoring is required, follow the established Quality Control procedures for your laboratory.
- If quality control results do not fall within an acceptable range defined by your laboratory, patient values may be suspect and corrective action should be taken.

Results
The result unit for the QMS Amikacin assay can be reported as µg/mL or µmol/L. To convert results from µg/mL amikacin to µmol/L amikacin, multiply µg/mL by 1.71.

As with all analyte determinations, the amikacin value should be used in conjunction with information available from clinical evaluations and other diagnostic procedures.

Result Error Codes
Some results may contain Result Error Codes. Refer to the instrument specific operations manual for a description of the error codes.

Limitations Of The Procedure
Interfering heterophile antibodies occur at a low frequency in the general population. These antibodies can cause autoagglutination of the microparticle reagent leading to undetected erroneously low results.

For diagnostic purposes, interfering heterophile antibodies occur at low frequency in the general population. These antibodies can cause auto-agglutination of the microparticle reagent leading to erroneous results that may be unexpectedly low or unexpectedly high. An erroneous result could lead to incorrect patient management; incorrect patient management could potentially cause serious injury or death. Test results should not be used in isolation to make patient management decisions. Results should always be assessed in conjunction with the patient's medical history, clinical examinations, and other clinicopathological findings. An alternative test method should be used to confirm results when results are inconsistent with clinical expectations.

See the SPECIMEN COLLECTION AND HANDLING and SPECIFIC PERFORMANCE CHARACTERISTICS sections of this package insert.

Expected Values
Although optimum values may vary, peak serum values of amikacin in the range of 20 to 25 µg/mL and trough values in the range of 5 to 10 µg/mL are generally accepted for therapeutic effectiveness.[9] Toxicity is associated with peak levels greater than 35 µg/mL and trough values greater than 10 µg/mL.[6] 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. Since amikacin is inherently stable, is not metabolized, and is excreted primarily by glomerular filtration, the presence of renal impairment drastically alters its pharmacokinetics. If dosage regimens are not drastically adjusted, excess accumulation leading to ototoxicity and further renal impairment could be encountered.[10-13] While serum levels can be toxic, indiscriminately low dosages of amikacin will result in ineffective treatment for many strains of gram-negative bacteria. Organisms resistant to amikacin often show increased resistance to all other available aminoglycosides. This observation points out the possibility that the indiscriminate use of low dosages of amikacin could engender the emergence of drug-resistant organisms and possibly render the drug ineffective in treating infectious disease.[5,14,15]

Specific Performance Characteristics
Representative performance results obtained on a commercially available automated clinical chemistry analyzer that employs turbidimetric quantitative analysis are shown below.

Least Detectable Dose (LDD) / Analytical Sensitivity
The LDD, or analytical sensitivity, of the QMS Amikacin assay is defined as the lowest measurable concentration that can be distinguished from zero with 95% confidence. The LDD was determined to be 0.8 µg/mL.

Assay Range
The range of the assay is 1.5 to 50.0 µg/mL.

Linearity
Each level of QMS Amikacin calibrator was diluted with equal volume of the next higher level calibrator to achieve samples at 1.5, 6.5, 15.0, 27.5 and 42.5 µg/mL. The samples were analyzed in duplicate using the QMS Amikacin assay. A mean of the replicates for each sample was determined and a percent recovery calculated. Results are shown below.

Theoretical Concentration (µg/mL)	Mean Recovered Concentration (µg/mL)	% Recovery
1.5	1.67	111.3
6.5	6.48	99.7
15.0	14.67	97.8
27.5	26.32	95.7
42.5	41.44	97.5

Mean percent recovery: 100.4

Method Comparison
Correlation studies were performed using NCCLS Protocol EP9-A.[16] Results from the QMS Amikacin assay on a Hitachi System were compared with results from a commercially available fluorescence polarization immunoassay. The patient samples consisted of serum and plasma. The amikacin concentrations ranged from 2.38 µg/mL to 37.58 µg/mL. Results of the Passing-Bablok regression analysis for the study are shown below.

Slope	1.00
Y-Intercept	0.25
Correlation Coefficient (R^2)	0.992
Number of Samples	56

Precision
Precision was determined as described in NCCLS protocol EP5-A.[17]
A tri-level human serum based commercial control containing amikacin was used in the study. Each level of control was assayed in duplicate twice a day for 20 days. Each of the runs per day was separated by at least two hours. The means were calculated, and the Within Run, Between Day, and Total SD and percent CVs were calculated. Representative results are shown below.

			Within Run		Between Day		Total	
Sample	N	Mean (µg/mL)	SD	CV (%)	SD	CV (%)	SD	CV (%)
1	80	4.09	0.22	5.37	0.19	4.77	0.41	9.94
2	80	12.00	0.21	1.79	0.08	0.70	0.74	6.22
3	80	24.37	0.47	1.93	0.40	1.65	1.54	6.32

Acceptance criteria: <10% total CV

Interfering Substances
The following compounds, when tested with the QMS Amikacin assay at the concentrations indicated, resulted in less than 10% error in detecting amikacin. Interference studies were conducted using NCCLS protocol EP7-P.[18] The results are shown below.

Interfering Substance	Interferent Concentration	N	Amikacin (µg/mL)	% Recovery
Total Protein	12 g/dL	3	24.03	96.0
Bilirubin	15 mg/dL	2	21.65	96.4
Hemoglobin	10 g/L	2	17.32	93.4
HAMA Type-1*	normal human level	2	20.41	100.5
HAMA Type-2*	normal human level	2	16.98	98.0
Triglyceride	1691 mg/dL	3	24.03	96.3

*HAMA = human anti-mouse antibodies

Specificity

Drug Cross-Reactivity

Cross-reactivity was tested with drugs that are routinely administered with amikacin. The following compounds were tested.

Compound	Compound Concentration (µg/mL)	Amikacin Concentration (µg/mL)	% Cross-Reactivity
5-Fluorocytosine	30	19.82	-0.39
Amphotericin	100	20.92	1.33
Ampicillin	50	19.50	ND
Carbenicillin	2500	20.25	ND
Cephalexin	320	20.16	ND
Cephalosporin C	1000	19.16	ND
Cephalothin	1000	20.79	ND
Chloramphenicol	250	20.98	0.55
Clindamycin	2000	18.44	ND
Erythromycin	500	19.71	ND
Ethacrynic acid	400	20.77	ND
Furosemide	100	20.60	1.00
Fusidic acid	1000	20.63	ND
Gentamicin	100	19.32	ND
Kanamycin A	400	19.23	ND
Kanamycin B	400	19.48	ND
Lincomycin	2000	21.09	ND
Methicillin	200	20.42	0.41
Methotrexate	500	15.64	ND
Methylprednisolone	200	20.87	0.64
Neomycin	1000	19.44	ND
Netilmycin	125	19.03	ND
Oxytetracycline	2000	20.24	ND
Penicillin V	100	20.98	1.38
Prednisolone	12	20.10	2.36
Rifampicin	500	19.84	ND
Spectinomycin	100	20.46	ND
Streptomycin	400	19.31	ND
Sulfadiazine	1000	19.72	ND
Sulfamethoxazole	400	20.00	ND
Tetracycline	2000	21.06	ND
Tobramycin	100	19.67	0.32
Trimethoprim	200	19.56	ND
Vancomycin	400	19.46	ND

*ND = Not Detectable

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Glossary:

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