QMS® Gentamicin (GENT)

thermo scientific

IVD **For In Vitro Diagnostic Use Only**

Rx Only

REF **10014390**
10017107

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® Gentamicin assay is intended for the quantitative determination of gentamicin in human serum or plasma on automated clinical chemistry analyzers.

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

Summary and Explanation of the Test

Gentamicin is used in the treatment of serious infections involving aminoglycoside-sensitive organisms.

Monitoring gentamicin concentration in serum or plasma, along with careful clinical assessment, is the most effective means of ensuring adequate therapy. Gentamicin concentration correlates better with antibacterial activity than dosage. A standard dose of gentamicin does not always yield a predictable concentration because drug concentration depends on patient's volume of distribution and on drug elimination. The mode of administration, the volume of extracellular fluid, renal retention, and physiological change influence these factors during therapy. Gentamicin has a narrow range of safe and effective concentration. Exposure to high concentrations for a prolonged period may cause renal impairment or ototoxicity. Patients with impaired renal function should be monitored closely while on gentamicin therapy because nephrotoxicity caused by gentamicin may be difficult to distinguish from symptoms of underlying renal disease.[1]

Principles of the Procedure

The QMS Gentamicin 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 gentamicin antibody reagent. The gentamicin-coated microparticle reagent is rapidly agglutinated in the presence of the anti-gentamicin 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 gentamicin 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 gentamicin concentration and the lowest agglutination rate at the highest gentamicin concentration.

Reagents

Reagent Kit

QMS Gentamicin, **REF** 10014390, or **REF** 10017107 is supplied as a liquid, ready-to-use, two-reagent kit that contains:

REF 10014390	**REF** 10017107
R1 Reagent 1 1 x 22 mL	**R1** Reagent 1 1 x 19 mL
R2 Reagent 2 1 x 9 mL	**R2** Reagent 2 1 x 8 mL
Barcoded C Pack Cartridge	Barcoded Indiko Kit

Reactive Ingredients

INGRED	Ingredient	Concentration
R1	Anti-gentamicin Monoclonal Antibody (Mouse)	<1.0%
	Sodium Azide	≤0.05%
R2	Gentamicin-coated Microparticles	≤0.4%
	Sodium Azide	≤0.05%

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.
- The reagents contain ≤0.2% bovine serum albumin (BSA). Avoid contact with skin and mucous membranes. Avoid inhalation. May cause topical or respiratory allergic reaction. Flush affected areas with copious amounts of water. In case of accident by inhalation, remove to fresh air and keep at rest.

DANGER: QMS Gentamicin (GENT) contains ≤5.0% Drug-specific antibody, ≤3.5% IgM, and ≤0.2% Bovine serum albumin (BSA).
H317 - May cause allergic skin reaction.
H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled.

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 Gentamicin assay:

	Glass	Plastic
Serum	• No Additive • Serum Separator Tube (gel) • Clot Activator	• With Silicon • Serum Separator Tube (gel) • Clot Activator
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 Gentamicin 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.[2]
- Samples for the QMS Gentamicin assay should be drawn just prior to a dose (trough level) to confirm that an adequate dose has been prescribed. Peak specimen should be drawn 30 minutes after a 30 minute IV infusion.[3] 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.

NOTE: Samples containing carbenicillin or piperacillin should be stored frozen if a delay in analysis of more than 8 hours is anticipated. Failure to freeze samples containing these antibiotics may result in falsely low gentamicin levels due to in vitro inactivation.[4]

Procedure

Materials Provided

- QMS Gentamicin Reagents, REF 10014390, or REF 10017107

Materials Required but not Provided

- QMS Gentamicin Calibrators, REF 0373902
  CAL A-F: 1 x 1.0 mL each
- Gentamicin Controls

Assay Procedure

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

Manual Dilution Protocol

A manual dilution can be performed on patient samples with gentamicin concentrations reported as greater than 10.0 µg/mL by making a dilution of the specimen with QMS Gentamicin 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 sensitivity of 0.3 µg/mL. The concentration reported must be multiplied by the manual dilution factor to obtain the final sample concentration.

$$\text{Final Sample Concentration} = \text{Reported Concentration} \times \text{Manual Dilution Factor}$$

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

Calibration

The QMS Gentamicin assay must be calibrated using a full calibration (6-point) procedure. To perform a full calibration, test the QMS Gentamicin 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: QMS Gentamicin 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 Gentamicin 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 Gentamicin assay can be reported as µg/mL or µmol/L. To convert results from µg/mL gentamicin to µmol/L gentamicin, multiply µg/mL by 2.09.[3]

As with all analyte determinations, the gentamicin 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

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

Patient samples which contain the drug sisomicin will yield falsely elevated values for gentamicin. See SPECIFICITY section for further explanation. However, this drug is not usually co-administered with gentamicin.

High concentrations of penicillins or cephalosporins have been shown to inactivate gentamicin in vitro. The degree of inactivation is dependent on the particular aminoglycoside being measured, the type and concentration of the penicillin or cephalosporin that is also present and the storage conditions of the sample.[5-7] Samples from patients receiving additional antibiotics of these types should be assayed immediately or stored frozen.

In very rare cases, patient samples may contain heterophile antibodies, which may produce low results with the QMS Gentamicin assay.

Interfering heterophile antibodies occur at 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.

Expected Values

Periodic measurements of both peak and trough concentrations of gentamicin are recommended to ensure adequate drug levels and prevention of toxic side effects. The gentamicin therapeutic range for moderate infections is considered to be 2 to 8 µg/mL.[8] Trough levels greater than 2 µg/mL have been associated with nephrotoxicity.[1] The 11 susceptibility of the infecting organism, the severity of the infection, and the general health of the patient should be considered when determining an adequate drug level for individual patients.

Example Trough and Peak[9]

	Less Severe Infection	Severe Infection	Toxic Levels
Trough (µg/mL)	<1	<2 to 4	>2 to 4
Peak (µg/mL)	5 to 8	8 to 10	>10 to 12

Specific Performance Characteristics

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

Sensitivity

Limit of Quantitation (LOQ)

The LOQ of the QMS Gentamicin assay is defined as the lowest concentration of an analyte that can be reliably detected and at which the total error meets accuracy requirements. The LOQ was determined to be 0.3 µg/mL.

Assay Range

The range of the assay is 0.3 to 10.0 µg/mL.

Accuracy

Accuracy was determined using a procedure described in guideline NCCLS EP6-A.[10] Each level of QMS Gentamicin calibrator was diluted with an equal volume of the next higher calibrator to yield mid-point samples of 1.00, 2.25, 4.50, and 8.00 µg/mL.

The samples were analyzed in triplicate using the QMS Gentamicin assay. A mean of the replicates for each sample was determined and percent recovery calculated. Representative results are shown below.

$$\text{Percent Recovery} = \frac{\text{Mean recovered concentration}}{\text{Theoretical concentration}}$$

Theoretical Concentration (µg/mL)	Mean Recovered Concentration (µg/mL)	% Recovery
1.00	1.09	109.0
2.25	2.37	105.0
4.50	4.60	102.2
8.00	8.23	102.9

Mean percent recovery: 104.8

Linearity

A gentamicin linearity standard was serially diluted and run in triplicate using the QMS Gentamicin 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
1.72	1.64	95.3
3.44	3.62	105.2
5.16	5.27	102.1
6.88	7.20	104.6

Mean percent recovery: 101.8

Method Comparison

Correlation studies were performed using NCCLS Protocol EP9-A2.[11] Results from the QMS Gentamicin assay were compared with results from a commercially available fluorescence polarization immunoassay. Results of the Passing-Bablok[12, 13] regression analysis for the study are shown below.

Slope	1.102
Y-Intercept	-0.412
Correlation Coefficient (R^2)	0.997
Number of Samples	63

Precision

Precision was determined as described in NCCLS protocol EP5-A2.[14]

A tri-level human serum based commercial control containing gentamicin 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, the between day, within run, and total SD 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	2.45	0.09	3.7	0.03	1.4	0.10	3.9
2	80	6.10	0.12	2.0	0.17	2.8	0.22	3.6
3	80	9.12	0.12	1.3	0.18	2.0	0.25	2.8

Acceptance criteria: <10% total CV

Interfering Substances

The following compounds, when tested with the QMS Gentamicin assay at the concentrations indicated, resulted in less than 10% error in detecting gentamicin. Interference studies were conducted using NCCLS protocol EP7-A2.[15] The results are shown below.

Interfering Substance	Interferent Concentration	N	Gentamicin (µg/mL)	% Recovery
Bilirubin	20 mg/dL	3	3.44	99.5
HAMA Type-1*	normal human level	2	3.33	99.1
HAMA Type-2*	normal human level	2	3.33	93.3
Hemoglobin	2 g/dL	3	3.44	98.3
Rheumatoid Factor**	1,240 IU/mL	3	3.56	97.8
Total Protein	12 g/dL	3	3.44	93.4
Triglyceride	1,691 mg/dL	3	3.44	95.8

*HAMA = human anti-mouse antibodies

**Patient samples containing Rheumatoid Factor levels above 1,240 IU may produce erroneous results with this assay.

Specificity

Cross-Reactivity

The aminoglycoside sisomicin cross-reacts with the QMS Gentamicin assay due to its structural similarity. Therefore, the results of this assay cannot be used to accurately quantify gentamicin serum or plasma levels in patients on sisomicin in combination with gentamicin.

Drug Cross-Reactivity

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

Compound	Compound Concentration (µg/mL)	Gentamicin Concentration (µg/mL)	% Cross-Reactivity
Acetaminophen	200	1.58	ND
Acetyl cysteine	1000	3.71	ND
Acetylsalycilic Acid	300	1.56	ND
Amikacin	300	3.76	ND
Amphotericin B	100	3.71	ND
Ampicillin	50	3.76	ND
Ascorbic Acid	30	3.76	-0.23
Carbenicillin	2500	3.71	ND
Cefamandole Nafate	250	3.76	ND
Cefoxitin	1000	3.71	ND
Cephalexin	320	3.76	ND
Cephalosporin C	1000	3.65	ND
Cephalothin	1000	3.71	ND
Chloramphenicol	250	3.71	ND
Clindamycin	2000	3.51	ND
Cyclosporine	6000	1.56	ND
Erythromycin	500	3.71	ND
Ethacrynic Acid	400	3.71	ND
5-Fluorocytosine	30	3.53	0.53
Furosemide	100	3.71	ND
Fusidic Acid	1000	3.71	ND
Ibuprofen	7000	1.58	ND
Kanamycin A	400	3.65	0.10
Kanamycin B	400	2.65	ND
Levodopa	1000	3.78	ND
Lincomycin	200	3.71	ND
Methicillin	20	3.71	ND
Methotrexate	5	3.69	ND
Methylprednisolone	200	3.71	ND
Metronidazole	1000	1.57	ND
Neomycin	1000	3.65	ND
Netilmycin	125	3.21	0.25
Oxytetracycline	2000	3.71	ND
Penicillin V	10	1.58	ND
Phenylbutazone	1000	1.58	ND
Prednisolone	12	3.71	-0.29
Rifampin	5	1.59	ND
Sisomicin	10	3.59	50.35
Spectinomycin	100	3.76	ND
Streptomycin	400	3.65	ND
Sulfadiazine	1000	3.76	ND
Sulfamethoxazole	400	3.76	ND
Tetracycline	2000	3.71	ND
Theophylline	200	1.55	ND
Ticarcillin	100	3.87	-0.44
Tobramycin	100	3.65	0.16
Trimethoprim	20	3.69	0.30
Vancomycin	400	3.65	ND

*ND = Not Detectable

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