QMS™ Teicoplanin (TEICO)

thermo scientific

IVD **For In Vitro Diagnostic Use Only**

REF **0374645**

CAUTION: FOR EXPORT USE ONLY.
NOT FOR SALE IN THE UNITED STATES.

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™ Teicoplanin assay is intended for the quantitative determination of teicoplanin in human serum or plasma on automated clinical chemistry analyzers as an aid in the management of patients receiving teicoplanin therapy.

Summary and Explanation of the Test

Teicoplanin is a glycopeptide antibiotic complex of the vancomycin ristocetin group, structurally related to vancomycin in that both contain a heptapeptide backbone.[1,2] Like vancomycin, teicoplanin inhibits cell-wall biosynthesis by interfering with peptidoglycan synthesis in gram-positive bacteria.[3] Teicoplanin is indicated for the treatment of moderate to serious infections caused by susceptible strains of bacteria such as staphylococci, streptococci, enterococci, bacilli and diphtheroids.[4]

Teicoplanin is normally more than 90% protein bound in circulation and exhibits protein-binding dependent elimination.[5] The majority of teicoplanin is excreted unaltered in the urine. In subjects with normal renal function, teicoplanin administered intravenously as a single dose has a circulation halflife in excess of 150 hours.[6] Urinary elimination of teicoplanin decreases with renal impairment.[7,8] In addition, wide inter-individual variation in clearance rate has been reported with renal impairment, especially in critically ill patients.[7-9] Patients with a history of intravenous drug abuse and burn patients have shown wide variations in pharmacokinetic parameters between individuals.[10,11] Since pharmacokinetics of teicoplanin may not correlate with renal function and there are wide variations between individuals, monitoring of serum levels of teicoplanin has been recommended as a means of determining the appropriate dosage regimen and to facilitate dosage adjustment.[8-12] Bioassay and HPLC have been used previously to quantitate circulating serum levels of teicoplanin.[13-16]

Principles of the Procedure

Overview of Technology

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

Reagents

Reagent Kit

QMS Teicoplanin, **REF** 0374645, is supplied as a liquid, ready-to-use, two-reagent kit that contains:

REF 0374645
R1 Reagent 1 1 x 21 mL
R2 Reagent 2 1 x 9 mL

Reactive Ingredients

INGRED	Ingredient	Concentration
R1	Anti-Teicoplanin Polyclonal Antibody (Sheep)	<5.0%
	Sodium azide	0.05%
R2	Teicoplanin-coated Microparticles	<1.0%
	Sodium azide	0.09%

Reagent Handling and Storage

- **R1**, **R2** Ready for Use.
- Before use, invert several times, avoiding the formation of bubbles.
- Remove air bubbles, if present in the reagent cartridge. 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.

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

DANGER: QMS Teicoplanin assay contains <5.0% Drug-specific Polyclonal Antibody (Sheep), ≤3.5% IgM Antisera (Goat) and ≤2.0% Human Serum Albumin (HSA).
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. Specific treatment (see First Aid information on product label and/or Section 4 of the SDS). 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.

Precautions for Users

- For in vitro diagnostic use.
- Do not mix materials from different kit lot numbers.
- Avoid the use of short drawn samples. Increased amounts of anticoagulant may produce erroneous results.
- The reagents contain ≤ 5% Anti-Teicoplanin antibody (ATa). 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.

⚠ **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.

The reagents contain less or equal to 0.09% sodium azide. Avoid contact with skin and mucous membranes. Flush affected areas with copious amounts of water. Get immediate medical attention for eyes, or if ingested. Sodium azide may react with lead or copper plumbing to form potentially explosive metal azides. When disposing of such reagents, always flush with large volumes of water to prevent azide build-up. Clean exposed metal surfaces with 10% sodium hydroxide.

Specimen Collection and Handling

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

Plasma	Serum
EDTA (K_2)	SST (Serum Separator Tube)
Lithium Heparin	Off-Clot
Sodium Heparin	
Sodium Citrate	

- Other specimen collection tubes have not been validated for use with the QMS Teicoplanin assay. Follow the manufacturer's processing instructions for all collection tubes.
- The use of short drawn samples may yield erroneous results. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy may exhibit increased clotting time.
- Inadequate centrifugation of the specimen may cause erroneous results.
- Ensure specimens are free of fibrin, red blood cells, and other particulate matter.
- Remove the plasma or serum from the cells, clots, 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.[17]

- Specimens may be stored up to 7 days at 2 to 8°C. If testing will be delayed more than 7 days, specimens may be stored frozen (-20 ± 5°C) up to 28 days prior to being tested.

Procedure

Materials Provided

REF	Kit Description
0374645	QMS Teicoplanin Reagents

Materials Required but not Provided

REF	Kit Description
0374652	QMS Teicoplanin Calibrators, CAL A: 1 x 2.0 mL each, CAL B-F: 5 x 1.0 mL each
0374660	QMS Teicoplanin Controls, Levels 1-3: 1 x 2.0 mL each

Assay Procedure

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

Calibration

The QMS Teicoplanin assay must be calibrated using a full calibration (6-point) procedure. To perform a full calibration, test the QMS Teicoplanin 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, corrective action should be taken.

Note: Teicoplanin 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 government regulations or accreditation requirements. Each laboratory should establish its own control ranges and calibration frequency.

Recommended control requirements for the QMS Teicoplanin 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, sample values may be suspect and corrective action should be taken.

Results

The result units for the QMS Teicoplanin assay are reported as µg/mL.

As with all analyte determinations, the teicoplanin 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

In very rare cases, patient samples may contain heterophile antibodies, which may produce low results with the QMS Teicoplanin assay. 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. All results above 50.0 µg/mL should be diluted in a 1:1 dilution using Calibrator A and rerun on the assay. The diluted assay result should be multiplied by 2.

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

Expected Values

Teicoplanin trough concentrations that are at least 10 µg/mL may optimize therapy in cases of severe infection.[18] The monitoring of teicoplanin levels is recommended for patients with impaired renal function, patients receiving prolonged treatment at high doses, patients receiving other drugs with nephrotoxic potential, and patients who have a history of intravenous drug abuse.[4] Trough serum concentrations should not exceed 60 µg/mL.[4]

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 Teicoplanin assay is defined as the lowest concentration for which acceptable inter-assay precision and recovery is observed. The LOQ was determined to be 3.0 µg/mL.

Assay Range

The range of the assay is 3.0 to 50 µg/mL.

Accuracy

Accuracy by recovery was determined by spiking teicoplanin into pooled human serum to achieve concentrations across the assay range and analyzing each spiked sample in replicates of 5. A mean of the replicates for each sample was determined and percent recovery calculated. Recovery at specific dilutions were considered acceptable if the percent recovery was 100% ± 10%. All samples within the assay range (3.0 to 50 µg/mL) are within this acceptable recovery range. Representative results are shown below.

$$\% \text{ Recovery} = \frac{\text{Mean Recovered Concentration}}{\text{Theoretical Concentration}} \times 100$$

Recovery across the assay range

Theoretical Concentration (µg/mL)	Avg. of 5 Reps (µg/mL)	% CV	% Recovery
47.98	46.86	3.4%	97.7%
36.04	35.54	2.0%	98.6%
24.11	23.90	1.6%	99.1%
12.04	11.68	1.6%	97.0%
6.02	5.69	2.4%	94.5%
3.02	3.19	3.2%	105.6%
1.51	1.81	6.2%	119.9%

Linearity

Linearity was performed using CLSI Protocol EP6-A[19] as a guideline. Linearity was determined by spiking teicoplanin into pooled human serum to achieve concentrations across the assay range and analyzing each sample in replicates of 5. A linear and polynomial fit for the data is determined. The difference between the fitted values of the polynomial and the line is considered acceptable if the deviation from linearity is less than or equal to 15%. Representative results are shown below.

Theoretical Concentration (µg/mL)	Avg. of 5 Reps (µg/mL)	Deviation from Linearity
48.82	46.42	-3.3%
36.58	36.05	3.7%
24.48	24.61	4.3%
12.23	12.03	-0.3%
6.13	5.88	-1.5%
3.07	3.20	4.2%

Method Comparison

Method comparison was performed using CLSI Protocol EP9-A2[20] as a guideline. Correlation results were obtained by measuring clinical patient samples with both the QMS Teicoplanin Assay and Innofluor Teicoplanin Assay System on the same day. A total of 100 samples were assayed. The results of the regression analysis are shown below.

Summary of Method Comparison

Methods	N	Deming		Passing-Bablok		R
		Slope (95% CI)	Intercept (95% CI)	Slope (95% CI)	Intercept (95% CI)	
QMS (3-100 µg/mL) vs. Innofluor	100	0.93 (0.89 to 0.96)	0.29 (-0.60 to 1.17)	0.94 (0.90 to 0.97)	0.17 (-0.50 to 0.76)	0.98

Additionally, a comparison of samples was made between the two versions (3-50 µg/mL vs. 3-100 µg/mL) of the QMS assay. The results are shown below.

Methods	N (Plotted/ Total)	Deming		Passing-Bablok		R
		Slope	Intercept	Slope	Intercept	
QMS (3-50 µg/mL) vs. QMS (3-100 µg/mL)	120/120	1.091	-1.078	1.087	-0.182	0.9957

Precision

Precision study was performed as described in CLSI Protocol EP5-A2[21]. A tri-level human serum based control containing teicoplanin 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 between day, between run, within run, and total percent CVs were calculated. The results of precision study are provided below.

Sample	Target Value (µg/mL)	N	Mean (µg/mL)	Within-Run % CV	Between-Run % CV	Between Day % CV	Total % CV
Control level 1	8.0	80	8.0	1.4%	1.3%	1.7%	2.5%
Control level 2	25.0	80	26.2	1.2%	1.6%	2.0%	2.8%
Control level 3	40.0	80	42.3	1.8%	2.7%	1.8%	3.7%

Interfering Substances

Interference studies were conducted for both endogenous and exogenous compounds using CLSI protocol EP7-A2[22] as a guideline. These compounds were tested to determine whether they affect the quantitation of teicoplanin concentration using the QMS Teicoplanin assay.

Endogenous Substances

The following compounds, when tested with the QMS Teicoplanin assay six times each in a spiked serum containing 30 µg/mL teicoplanin at the concentrations indicated, resulted in less than 10% error in detecting teicoplanin. Results are shown below.

Interfering Substance Tested	Concentration Tested	Measured Test Sample (µg/mL)	% Recovery
Total Protein	> 12 g/dL	28.70	96.71
Bilirubin	21 mg/dL	31.29	103.06
HAMA Type 1*	Normal Human Level	31.08	102.37
HAMA Type 2*	Normal Human Level	31.46	103.61
Triglycerides	1526 mg/dL	30.31	99.84
Cholesterol	500 mg/dL	30.41	98.19
Hemoglobin	200 mg/dL	29.80	95.19
Rheumatoid Factor	502 IU/mL	30.73	97.44
Uric Acid	21 mg/dL	29.77	91.70
Oxalic Acid	0.8 mg/dL	30.11	99.95

*HAMA = human anti-mouse antibodies

Drug Interference

Cross-reactivity was tested with drugs that could be administered with teicoplanin. Cross-reactants were tested with the QMS Teicoplanin assay at the concentrations indicated in a spiked serum containing 30 µg/mL teicoplanin. The samples were assayed and the teicoplanin concentrations of the spiked samples were compared to a control serum. Results are shown below.

Compound Tested	Concentration Tested (µg/mL)	% Cross-Reactivity
Acetylsalicylic Acid	686	ND
Acetaminophen	201	ND
Amikacin	150	ND
Amphotericin B	105	ND
Ampicillin	57	ND
Arbekacin	66	ND
Bendroflumethiazide	498	ND
Caffeine	101	ND
Carbenicillin	252	ND
Cefamandole Nafate	253	-0.31
Cefazolin	508	ND

Table continued

Cephalexin	108	0.65
Cephalosporin C	1022	-0.14
Cephalothin	154	ND
Chloramphenicol	251	ND
Chlorothiazide	38	ND
Clindamycin	58	ND
Dipotassium EDTA	5414	ND
Compound Tested	**Concentration Tested (µg/mL)**	**% Cross-Reactivity**
Erythromycin	200	ND
Ethacrynic Acid	438	-0.13
Ethambutol	24	ND
5-Fluorocytosine	391	ND
Furosemide	107	-0.57
Fusidic Acid	922	ND
Gentamicin	22	ND
Hydrochlorothiazide	42	-1.92
Ibuprofen	448	0.15
Isoniazid	73	ND
Kanamycin A	63	ND
Kanamycin B	61	ND
Lincomycin	2138	ND
Methotrexate	910	-0.09
6α-Methylprednisolone	202	ND
Nalidixic Acid	515	ND
Naproxen	1007	ND
Neomycin	1154	ND
Niacin	831	0.05
Nitrofurantoin	119	ND
Oxytetracycline	2101	-0.03
Penicillin G	138	ND
Penicillin V	104	ND
Phenacetin	201	-0.31
Phenytoin	106	ND
Prednisolone	13	4.51
Prednisone	12	6.58
Rifampin	55	-14.24
Salicylic Acid	505	-0.29
Sisomicin	101	ND
Sodium Fluoride	22	ND
Spectinomycin	108	ND
Sulfadiazine	228	ND
Sulfamethoxazole	405	-0.19
Sulfisoxazole	298	0.28
Tetracycline	17	3.40
Tobramycin	26	ND
Trimethoprim	21	ND
Trisodium Citrate	506	ND
Vancomycin	636	0.22

ND = Not Detectable. The cross-reactivity is considered not detectable if the difference between the spiked sample and the control is less than the standard deviation of the control replicates.

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