QMS® Tacrolimus Immunoassay

thermo scientific

Rx Only

REF 10015556

For *In Vitro Diagnostic* Use Only

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 Tacrolimus Immunoassay is intended for the quantitative determination of tacrolimus in human whole blood on automated clinical chemistry analyzers. The results obtained are used as an aid in the management of kidney, liver, and heart transplant patients receiving tacrolimus therapy. This *in vitro* diagnostic device is intended for clinical laboratory use only.

SUMMARY AND EXPLANATION OF TEST

Tacrolimus (FK506, PROGRAF®) is a macrolide antibiotic of fungal origin, *Streptomyces tsukubaensis,* with a potent immunosuppressive function as prescribed for patients with kidney and liver transplantation.[1] Tacrolimus is an inhibitor of calcineurin, which is a phosphatase in nature and activates T cell proliferation.[2-4] In cellular events, tacrolimus binds a family of binding protein termed FKBPs (FK506 binding proteins), and then forms a pentameric complex including tacrolimus, FKBP, calcineurins A and B, and calmodulin.[2-5] The pentamer formation results in the inhibition of phosphatase activity of calcineurin, which is required to activate transcriptional factors for transport into the cell nucleus. Thus, the gene expression of T-lymphocytes is impaired especially for cytokines such as IL-2 and results in an immunosuppressive effect in patients.[2-5]

The distribution of tacrolimus between whole blood and plasma depends on several factors, such as hematocrit, drug concentration, and plasma protein concentration. The ratio of whole blood to plasma concentration averaged 35 (range 12 to 67).[6-7] Tacrolimus is extensively metabolized by the cytochrome P-450 system mainly CYP3A.[8-11] The drug is metabolized into at least 8 metabolites (M-I – M-VIII) through demethylation and hydroxylation.[12] The average half-life of tacrolimus in-vivo is estimated as 48 hours.[8-11] It was also reported that there were large intra-patient variability as well as inter-patient variability in tacrolimus concentrations in whole blood.[13] Careful and frequent monitoring of tacrolimus is recommended.[14]

PRINCIPLES OF THE PROCEDURE

The QMS Tacrolimus Immunoassay 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 tacrolimus antibody reagent. The tacrolimus-coated microparticle reagent is rapidly agglutinated in the presence of the anti-tacrolimus antibody reagent and in the absence of any competing drug in the sample. The rate of absorbance change is measured photometrically at 700 nm. When a sample containing tacrolimus 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 the maximum rate of agglutination at the lowest tacrolimus concentration and the lowest agglutination rate at the highest tacrolimus concentration.

REAGENTS

Reagent Kit

QMS Tacrolimus, **REF** 10015556, is supplied as a liquid, ready-to use, three-reagent kit that contains:

REAGENT 1 1 x 18 mL

REAGENT 2 1 x 12 mL

EXT Extraction Reagent 1 x 50 mL (working solution required, see p. 2, Extraction Solution Preparation)

Reactive Ingredients

INGRED	Ingredient	Concentration
REAGENT 1	Anti-Tacrolimus Monoclonal Antibody (Rabbit)	<1.0%
	Sodium Azide	0.09%
REAGENT 2	Tacrolimus-coated Microparticles	<0.3%
	Sodium Azide	0.09%
EXT	Sodium Azide	0.09%

REAGENT HANDLING AND STORAGE

- **REAGENT 1**, **REAGENT 2**, and **EXT** (Extraction Reagent) 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 **REAGENT 1** or the **REAGENT 2** cartridge becomes empty, replace both cartridges and verify calibration with at least one sample of each level of controls according to the established Quality Control requirements for your laboratory. If control results fall outside acceptable ranges, recalibration may be necessary.
- Refer to the analyzer specific Assay System Parameter Sheet for system specific information.
- In the case of accidental spill, clean and dispose of material according to your laboratory's SOP, local, and state regulations.
- In the case of damaged packaging on arrival, contact your technical support representative (refer to back page of this PI).

⚠ **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

- For *In Vitro* Diagnostic Use Only. Exercise the normal precautions required for handling all laboratory reagents.
- Do not mix materials from different kit lot numbers.
- Do not use reagent kits beyond the expiration date.

DANGER: QMS Tacrolimus Immunoassay contains ≤3.0% human serum albumin (HSA) and ≤1.0% Drug-specific antibody (Rabbit).
QMS Tacrolimus Extraction reagent contains ≤9.0% zinc sulfate (ZnSO4).
H317 - May cause allergic skin reaction.
H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled.
H318 - Causes serious eye damage.
H411 - Toxic to aquatic life with long-lasting effects.

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.

Avoid release to the environment. Wear protective gloves/eye protection/face protection. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a Poison Center or doctor/ physician. Collect spillage. Dispose of contents/container to location in accordance with local/regional/national/international regulations.

⚠ **CAUTION:** Materials of human origin were tested for HIV1 and 2, Hepatitis B and Hepatitis C by FDA approved method, and the findings were negative. However, as no test method can rule out the potential risk of infection with absolute certainty, the material must be handled just as carefully as a patient sample. In the event of exposure, the directives of the responsible health authorities should be followed.

Reagents used in the assay components contain ≤0.09% sodium azide. Avoid contact with skin and mucous membranes. Refer to SDS for additional precautions, handling instructions, and accidental exposure treatment.

SPECIMEN COLLECTION AND HANDLING

- Only whole blood specimens collected in EDTA tubes may be used. Follow the manufacturer's processing instructions for all collection tubes. Care should be taken to preserve the integrity of the specimen from the time of collection until performance of the assay. Specimens should be labeled with both the time of blood collection as well as the last drug administration.
- Specimens should be capped and assayed within 7 days when stored at 2-8°C or within 6 months when stored at ≤ -20°C.[6,10-11] Avoid repeated freezing and thawing. Do not induce foaming of samples.

PROCEDURE

Materials Provided

- QMS Tacrolimus Reagent Kit, REF 10015556

Materials Required but not Provided

- QMS Tacrolimus Calibrators, REF 10015573, CAL A: 1 x 4 mL, CAL B-F: 1 x 2 mL each
- Quality Control Products
  Materials Recommended:
  - MORE Diagnostics Rap/Tac/CsA Controls,
    LOW, 280-Q: 4 x 4 mL each
    MID, 280-1: 4 x 4 mL each
    HIGH, 280-2: 4 x 4 mL each
  - For other commercially available quality control products call Thermo Fisher Scientific Technical Support
- Methanol, HPLC grade (≥ 99.8% purity)
- Round bottom Microcentrifuge tubes
- Automated clinical chemistry analyzer

Sample Preparation

Note: Please follow vendor-specific package insert instructions and handling recommendations, if provided, for controls.

Allow calibrators and patient specimens to equilibrate to room temperature before extraction. Calibrators should mix for a minimum of 15-20 minutes and patient specimens should be thoroughly mixed at room temperature prior to use. Mix calibrators and patient specimens well by gentle inversion (use of a rocker is preferred). Avoid the formation of bubbles.

Extraction Solution Preparation

1. Add exactly 10 mL of room temperature Extraction Reagent to a clean, dry, airtight bottle.
2. Add exactly 40 mL of HPLC Grade Methanol (≥ 99.8% purity) to the bottle and gently mix. Label this as "Tacrolimus Working Extraction Solution." Record the current date, and date of expiration (2 weeks from date of preparation) on the label. Store at room temperature.

Extraction Procedure for Samples, Calibrators, and Controls

FOR OPTIMAL RESULTS, FOLLOW THE STEPS BELOW PRECISELY. EXTRACTS MUST BE RUN IMMEDIATELY AFTER EXTRACTION.

1. Prepare and label round bottom microcentrifuge tubes for extraction of samples, calibrators and controls. Prepare one microcentrifuge tube for each sample.
2. Use a pipette to measure exactly 200 µL of sample, calibrator or control materials into the labeled microcentrifuge tube. Aspirate the sample with the pipette, gently wipe the pipette tip on the edge of the sample vial to remove any access sample, then dispense the sample into the inside wall of the microcentrifuge tube. **Note:** Check the pipette tip to ensure no air bubbles are in the tip. Air in the tip is a potential source for imprecision.
3. Use a pipette to measure exactly 200 µL of extraction solution into the microcentrifuge tube. When preparing multiple samples, a repeater pipette is recommended to aspirate and dispense the extraction solution. Remove any air bubbles in the pipette tip prior to dispensing the extraction solution.
4. Cap and vortex the microcentrifuge tube at maximum speed immediately for 15-30 seconds. Inspect each tube for a homogeneous mixture. If un-mixed sample is detected, dislodge the un-mixed portion and re-vortex.
5. Let the mixture in the microcentrifuge tube sit at room temperature for 5-7 minutes.
6. Place the microcentrifuge tube into a centrifuge and centrifuge for 5 minutes at an RPM equivalent to 15,000 - 16,000 xg.
7. Decant the supernatant into a sample cup (avoid the formation of bubbles) and immediately run the measurement to minimize sample evaporation. Do not tap the cup to release the last drop in a way that could disturb the pellet.
8. Dispose of extracts after analysis. Retesting of samples requires fresh extractions.

Note: Additional tips and recommendations of sample extraction steps for the QMS Tacrolimus Immunoassay are also available from Thermo Fisher Scientific Technical Support.

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 Tacrolimus CAL A (0.0 ng/mL) to manually dilute samples outside the linearity of the assay.

Manual Dilution Protocol

A manual dilution can be performed on patient samples with tacrolimus concentrations reported as greater than 30 ng/mL by making a 1:1 dilution of the specimen with QMS Tacrolimus CAL A (0.0 ng/mL) before extracting the sample. The dilution must be performed so the diluted test result reads greater than the assay sensitivity of 1 ng/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

Manual Dilution Factor = (Volume of Sample + Volume of CAL A) ÷ Volume of Sample

CALIBRATION

The QMS Tacrolimus Immunoassay must be calibrated using a full calibration (6-point) procedure. To perform a full calibration, test the QMS Tacrolimus Calibrators A, B, C, D, E, and F. Only QMS Tacrolimus Calibrators should be used with the QMS Tacrolimus Immunoassay. Accurate quantitative determination of tacrolimus cannot be obtained if the QMS Tacrolimus Calibrators set, REF 10015573, is not used in calibration of the QMS Tacrolimus Immunoassay.

Calibration is required with each new lot number. Verify the calibration curve with at least one sample of each level of controls according to the established Quality Control requirements for your laboratory. If control results fall outside acceptable ranges, corrective action should be taken.

Calibration Frequency

Recalibration is recommended

- After calibrator or reagent (kit) lot change
- After performance of monthly instrument maintenance
- As required following quality control procedures

QUALITY CONTROL

All quality control requirements should be performed in conformance with local, state and/or federal regulations or accreditation requirements.

As appropriate, refer to your laboratory Standard Operating Procedure(s) and/or Quality Assurance Plan for additional quality control requirements and potential corrective actions.

Recommended control requirements for the QMS Tacrolimus Immunoassay:

- A minimum of one sample of each level of controls should be run each time patient samples are extracted and assayed.
- If more frequent control monitoring is required, follow the established Quality Control procedures for your laboratory.
- All quality control requirements should be performed in conformance with local, state and/or federal guidelines.
- If quality control results do not fall within an acceptable range defined by your laboratory, patient values may be suspect and should not be reported. Corrective action should be taken.

RESULTS

The result units for the QMS Tacrolimus Immunoassay are reported as ng/mL.

Reporting Results: Laboratories should report that the results are obtained by the QMS Tacrolimus method.

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

- The concentrations of tacrolimus in a given specimen determined with assays from different manufacturers can vary due to differences in assay methods and reagent specificity. Monitoring with one assay consistently is recommended.
- **Immunoassays are non-specific and cross-react with metabolites. Because of this immunoassays may overestimate the concentration of tacrolimus (see Method Comparison section). When elimination of tacrolimus is impaired metabolites may accumulate to a greater extent leading to a greater overestimation. In such cases use of a specific assay (e.g. chromatographic method) should be considered.**
- Interfering heterophile antibodies occur at a low frequency in the population. These antibodies can lead to erroneous results (including erroneously low results caused by agglutination of the microparticle reagent).

- The test findings should always be assessed in conjunction with the patient's medical history, clinical examinations and other findings. Additional testing to confirm results should be performed when results are inconsistent with clinical evidence.
- Refer to the PROGRAF package insert regarding effects of co-administered drugs, and drugs that may increase or decrease tacrolimus concentrations.[14]

EXPECTED VALUES

The optimal therapeutic range for tacrolimus in whole blood has not been established with this assay. The therapeutic ranges for tacrolimus may vary depending on clinical factors and on the methodology used.

Given the heterogeneity of the patient's clinical state, clinicians should establish a desired therapeutic management range based on their own experience as well as each patient's clinical requirements. Changes to treatment regimen should not be based solely on tacrolimus values. Differences in sensitivity to immunosuppressive and nephrotoxic effects of tacrolimus, co-administration of other immunosuppressants, type of transplant, time post-transplant and a number of other factors contribute to different requirements for optimal blood levels of tacrolimus.

Optimal ranges may vary depending on the test used, and therefore should be established for each commercial test. Values obtained with different assay methods cannot be used interchangeably due to differences in methodology and cross reactivity, nor should correction factors be applied. Consistent use of one assay for individual patients is recommended.

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance results obtained on a commercially available automated clinical chemistry analyzer that employs turbidimetric quantitative analysis are shown below. Unless otherwise stated all assays were conducted in accordance with the assay procedure provided herein using the Beckman AU680 analyzer. Results obtained in individual laboratories may differ from these data. For additional analyzer specific performance data, refer to the analyzer specific application protocol or call Thermo Fisher Scientific Technical Support for assistance.

Reportable Range

The reportable range for the QMS Tacrolimus Immunoassay is 1 ng/mL (minimum reportable value based on Functional Sensitivity) to 30 ng/mL tacrolimus.

Functional Sensitivity (Limit of Quantitation)

The functional sensitivity represents the lowest tacrolimus concentration that can be measured with an inter-assay precision at 20% CV. The study was carried out using whole blood specimens spiked with tacrolimus ranging from 0.5 to 5.0 ng/mL for one measurement per run, twice a day, for 30 days with a total of 60 data points. At the upper 95% confidence limit, the LoQ was calculated to be 0.9 ng/mL, which supports the lower assay limit of 1.0 ng/mL. The observed percentage recovery at 0.9 ng/mL is 102.0%.

Dilution Linearity

A linearity study was performed by diluting a high concentration tacrolimus sample with the QMS Tacrolimus Calibrator A to concentrations evenly distributed across the assay range. The percent recovery was determined by dividing the measured tacrolimus concentration by the expected concentration. The expected concentrations were determined using the high concentration tested multiplied by a dilution factor.

% of High Sample	Expected Concentration (ng/mL)	Measured Concentration (ng/mL)	Recovery (%)
100.0%	29.9	29.9	100.0%
90.0%	26.9	26.0	96.8%
80.0%	23.9	22.8	95.4%
70.0%	20.9	19.2	91.8%
60.0%	17.9	17.2	96.1%
50.0%	14.9	14.7	98.6%
40.0%	12.0	11.1	92.7%
30.0%	9.0	8.6	95.7%
20.0%	6.0	6.0	100.0%
10.0%	3.0	3.1	102.9%
5.0%	1.5	1.5	100.4%
3.3%	1.0	1.0	101.4%
2.8%	0.8	0.8	99.6%
0.0%	0.0	0.0	N/A

Expected Concentration = % of High Sample x High Measured Concentration
Recovery (%) = (Measured Concentration ÷ Expected Concentration) x 100

Recovery

Negative whole blood samples were spiked with known amounts of tacrolimus at concentrations across the assay range. The tacrolimus concentrations of these samples were verified by an LC-MS/MS and tested with the QMS Tacrolimus Immunoassay. The results are shown below.

Sample ID	n	Expected Concentration (ng/mL)	Measured Concentration (ng/mL)	Recovery (%)
Sample 1	21	2.7	2.7	101.8
Sample 2	21	9.8	10.8	109.4
Sample 3	21	18.0	17.7	98.2
Sample 4	21	19.8	21.3	107.5
Sample 5	21	27.0	27.1	100.4

Recovery (%) = (Measured Concentration ÷ Expected Concentration) x 100

Precision

Precision was evaluated using whole blood pooled patient and spiked samples. The study was conducted as described in CLSI protocol EP5-A2.[15] Each sample was assayed in duplicates per run, twice a day for 20 days. The mean, the within-run and total-run SD and %CV were calculated. Representative results are shown below.

Samples	n	Mean (ng/mL)	Within-Run		Total-Run	
			SD	%CV	SD	%CV
Spiked Sample A	80	3.0	0.2	4.9%	0.2	7.1%
Spiked Sample B	80	10.0	0.2	1.9%	0.4	3.6%
Spiked Sample C	80	20.9	0.4	1.9%	1.1	5.0%
Patient Sample A	80	3.2	0.1	4.1%	0.2	6.2%
Patient Sample B	80	10.4	0.2	2.2%	0.4	3.6%
Patient Sample C	80	24.2	0.5	2.1%	1.1	4.6%

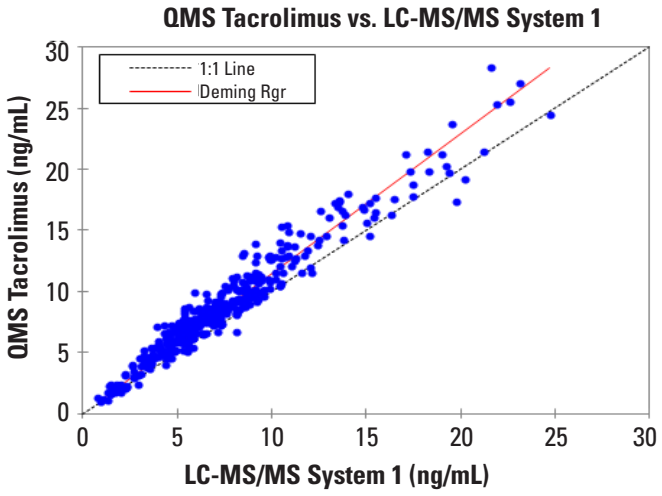
Method Comparison

Correlation studies were performed to compare the QMS Tacrolimus Immunoassay to two LC-MS/MS methods (System 1 and System 2) and the Abbott ARCHITECT® Tacrolimus Assay. The studies used human whole blood EDTA specimens obtained from kidney, liver and heart transplant patients taking tacrolimus. All tested specimens were trough samples from mainly adult patients with time of post-transplant for the samples generally > 9 months. The patients tested received drug regimens of Tacrolimus either alone or coadministered with other immunosuppressive drugs, mainly Mycophenolate Mofetil (MMF), Mycophenolic Acid (MPA), or Corticosteroids. The results of the Deming regression analysis[16] between the different methods are shown in the table below.

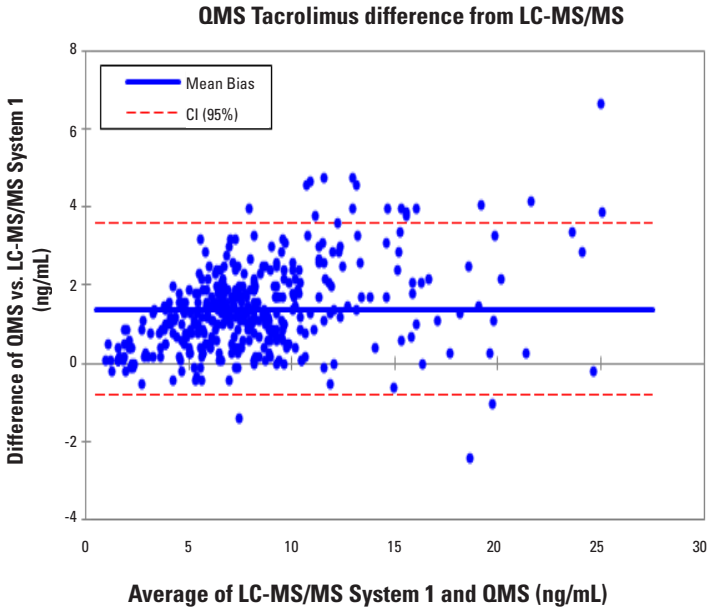
Comparative Method	n	Slope (95% CI*)	Intercept (95% CI)	Correlation Coefficient (R)
LC-MS/MS System 1	383	1.111 (1.084 to 1.137)	0.53 (0.31 to 0.76)	0.972
LC-MS/MS System 2	232	1.130 (1.092 to 1.167)	0.71 (0.42 to 1.01)	0.967
Abbott ARCHITECT Tacrolimus Assay	208	1.126 (1.071 to 1.181)	-0.03 (-0.63 to 0.56)	0.937

*Confidence Interval (CI)
QMS Tacrolimus Specimen Range: 1.0 to 30.8 ng/mL
LC-MS/MS Specimen Range: 0.8 to 29.5 ng/mL
ARCHITECT Tacrolimus Specimen Range: 2.4 to 28.1 ng/mL

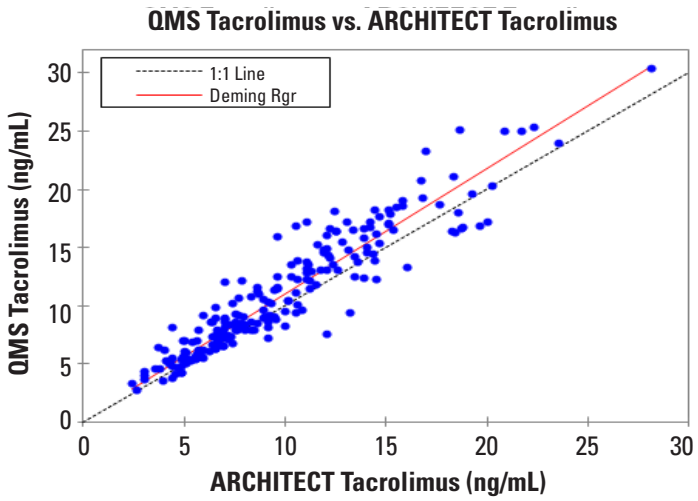
Scatter plot for results from QMS Tacrolimus vs LC-MS/MS System 1 for combined kidney, liver, and heart transplant samples.



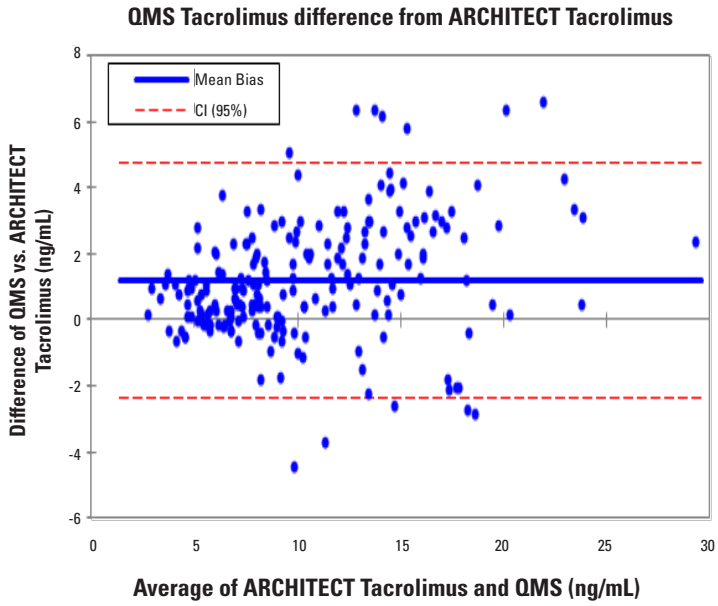
Bland and Altman bias plot[17] for results from QMS Tacrolimus vs LC-MS/MS System 1 for combined kidney, liver, and heart transplant samples. The Mean Bias is calculated as the average difference between the QMS Tacrolimus Immunoassay and LC-MS/MS System 1 results.



Scatter plot for results from QMS Tacrolimus vs Abbott ARCHITECT Tacrolimus for combined kidney and liver transplant samples.



Bland and Altman bias plot[17] for results from QMS Tacrolimus vs Abbott ARCHITECT Tacrolimus assay for combined kidney and liver transplant samples. The Mean Bias is calculated as the average difference between the QMS Tacrolimus Immunoassay and ARCHITECT Tacrolimus results.



Specificity

The specificity studies were conducted using CLSI protocol EP7-A2 as a guideline.[18] Cross-reactivity was tested for the available major metabolites of tacrolimus. Other medications routinely administered with tacrolimus were tested to determine whether these compounds affect the quantitation of tacrolimus using the QMS Tacrolimus Immunoassay.

The cross-reactivity of the metabolites was calculated using the formula:

$$\text{Cross-Reactivity (\%)} = \frac{\text{Measured concentration - Expected concentration}}{\text{Cross Reactant concentration}} \times 100$$

Cross-reactivity with tacrolimus metabolites

The cross-reactivity of the QMS Tacrolimus Immunoassay to major tacrolimus metabolites is presented in the following table. The compounds tested were added to human whole blood samples containing two concentrations of tacrolimus drug and tested in replicates of three. Percent of cross-reactivity was calculated.

Tacrolimus Metabolites	Metabolite Concentration (ng/mL)	Expected Concentration (ng/mL)	Measured Concentration (ng/mL)	Recovery (%)	Cross Reactivity (%)
M-I (13-O-demethyl)	20	5.8	7.6	131.0	9.2
	20	13.3	14.8	111.3	7.7
M-II (31-O-demethyl)	20	5.7	5.9	103.5	0.7
	20	13.2	13.1	99.2	-0.5
M-III (15-O-demethyl)	20	5.3	6.0	113.2	3.8
	20	12.4	13.0	104.8	2.7
M-IV (12-hydroxyl)	3.5	14.6	18.7	128.1	117.1
	3.3	21.2	27.0	127.4	174.8
	20	5.0	6.1	122.0	5.7
	20	12.0	14.1	117.5	10.5
M-VII (13,15-O-didemethyl)	20	5.4	7.3	135.2	9.3
	20	13.4	14.7	109.7	6.7
M-VII (13,15-O-didemethyl) + M-VI (13,31-O-didemethyl)	20	5.4	5.8	107.4	2.2
	20	13.4	13.8	103.0	2.0

Recovery (%) = (Measured Concentration ÷ Expected Concentration) x 100

The observed cross reactivity of Tacrolimus Metabolite M-IV was ≤ 174.8%. Tacrolimus Metabolite M-V and M-VIII have not been assessed to determine possible cross-reactivity.

Tacrolimus patient samples contain low concentrations of tacrolimus metabolites in comparison to the parent drug, with about 6% of M-I, 15% of M-II, 6% of M-III and nearly undetectable M-IV. [9,12,19]

Interfering Substances

Interference studies were conducted using CLSI protocol EP7-A2 as a guideline.[18] The QMS Tacrolimus Immunoassay was tested with tacrolimus co-administrated drugs and common drugs to see if there is any potential interference. The compounds tested were added to human whole blood samples containing approximately 5 and 12 ng/mL of tacrolimus drug and tested using the QMS Tacrolimus Immunoassay. Recovery of tacrolimus concentration greater than 10% error was considered to have interference with the assay. The compounds tested at the concentrations listed in the table below exhibit no interference with the assay. The average percentage recovery of tacrolimus ranged from 91% to 109%.

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
Acetaminophen	200,000	Kanamycin B Sulfate	100,000
Acycloguanisine / Acyclovir	1,000,000	Ketoconazole	100,000
Allopurinol	50,000	Labetalol	17,100
Amikacin Sulfate	150,000	Lidocaine	100,000
Amphotericin B	100,000	Lithium	35,000
Ampicillin	100,000	Lovastatin	20,000
Apresoline / Hydralazine	100,000	Methylprednisolone	100,000
Atenolol	40,000	Metoclopramide	100,000
Azathioprine	100,000	Minoxidil	60,000
Azithromycin	5,000	Morphine Sulfate	100,000
Bromocriptine / 2-Bromo-α-ergocryptine	8,000	Mycophenolic acid	100,000
Carbamazepine	120,000	N-Acetylprocainamide	120,000

Table Continued

Compound	Concentration (ng/mL)	Compound	Concentration (ng/mL)
Cefazolin	150,000	Nadolol	1,200
Ceftriaxone	500,000	Naproxen	100,000
Cephalosporin C	100,000	Nicardipine	500
Chlopromazine	50,000	Nicotine	20,000
Chloramphenicol	250,000	Nifedipine	100,000
Chlorodiazepoxide	20,000	Penicillin G	100,000
Chloroquine	1,500	Pentobarbital	100,000
Cimetidine	100,000	Phenobarbital	150,000
Ciprofloxacin	7,400	Phenytoin	100,000
Clarithromycin	5,000	Prazosin	100,000
Clonidine	100	Prednisolone	100,000
Colchicine	90	Prednisone	100,000
Cortisone	1,200	Primidone	100,000
Cyclosporine / Cyclosporin A	10,000	Probucol	600,000
Diazepam	20,000	Procainamide	100,000
Digitoxin	100,000	Propoxyphene	4,000
Digoxin	10,000	Propranolol	40,000
Diltiazem	60,000	Quinidine	100,000
Disopyramide	100,000	Ranitidine	200,000
Erythromycin	200,000	Rifampin / Rifampicin	100,000
Ethosuximide	300,000	Salicylic Acid	500,000
Everolimus	100	Sirolimus (Rapamycin)	300
Famotidine	10,000	Spectinomycin	100,000
Fluconazole	100,000	Streptomycin	100,000
Flucytosine / 5-Fluorocytosine	40,000	Sulfamethoxazole	150,000
Furosemide	100,000	Theophylline	250,000
Ganciclovir	1,000,000	Ticlopidine	150,000
Gemfibrozil	100,000	Tobramycin	100,000
Gentamicin	120,000	Triamterene	100,000
Hydrochlorothiazide	40,000	Trimethoprim	40,000
Hydrocortisol	100,000	Valproic Acid	500,000
Ibuprofen	400,000	Vancomycin	100,000
Itraconazole	100,000	Verapamil	100,000
Kanamycin A Sulfate	100,000		

The following potentially interfering endogenous substances, when tested with the QMS Tacrolimus Immunoassay at the concentrations indicated exhibited 92% to 108% recovery.

Potential Interfering Substance	Concentration
Albumin	12 g/dL
Bilirubin	60 mg/dL
Cholesterol	500 mg/dL
Creatinine	5 mg/dL
Triglyceride	1500 mg/dL
Uric Acid	20 mg/dL
IgG Gamma Globulin	12 g/dL
Rheumatoid Factor	500 IU/mL
HAMA*	400 ng/mL
Hematocrit	12% - 64%

*HAMA = human anti-mouse antibodies

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