thermoscientific

Thermo Scientific reagents for immunosuppressant drug testing

Complete solutions for patient monitoring

ThermoFisher SCIENTIFIC

Thermo Scientific™ QMS™
Everolimus Immunoassay

Accurate: Correlates well with gold standard method LC-MS/MS

Efficient: Excellent accuracy across assay range

Rapid: Quick turn-around-time

Limit Of Quantitation (LOQ): 2 ng/mL

Reportable Range: 2 to 20 ng/mL

Reference Method Comparison

Hitachi™ Analyzer vs. LC-MS/MS

Sample Type	N	Passing Bablok Regression		Correlation Coefficient (r)
		Slope	Intercept	
Kidney	150	1.11	-0.01	0.96
Liver	111	0.98	-0.06	0.93
Heart*	41	1.00	-0.15	0.96

* Heart indication is ex-US only

A correlation study was performed using 178 samples from adult liver transplant recipients. Results from the QMS Everolimus assay were compared with results from LC-MS/MS methods; both methods were used in the everolimus drug trial for liver transplantation.

Summary Method Comparison Regression Analysis with Liver Transplant Patient Samples

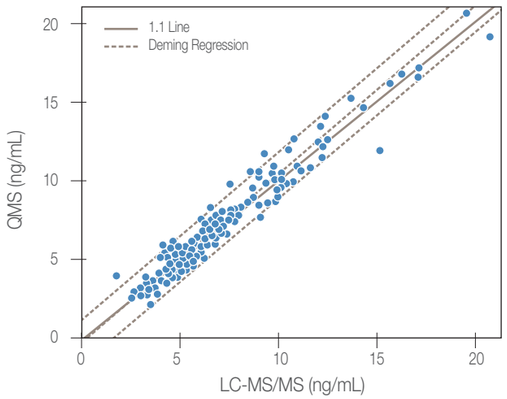
		Deming		
Method	N	Slope 95% CI	Intercept 95% CI	R
LC-MS/MS System 3 vs. QMS	178	1.02 (0.99 to 1.06)	0.15 (-0.11 to 0.40)	0.97

	Avg Bias (ng/mL)	Bias SD	Avg. % Bias
LC-MS/MS System 3 vs. QMS	0.29	0.76	4.00

Method Comparison

Samples: 178 liver transplant patient samples were analyzed using the Thermo Scientific QMS Everolimus Immunoassay vs. LC-MS/MS method.

Deming Regression Analysis: Slope was 1.02, and intercept was 0.15 with a correlation coefficient of 0.97.



Ordering: for IVD use

Item Number	Description	Format
10015987	QMS Everolimus Immunoassay	R1 22 mL, R2 8 mL
380005	QMS Everolimus Calibrator Set	6 levels, 3 mL 1 vial each
380010	QMS Everolimus Control Set	3 levels 3 mL 1 vial each

Ordering: for use in the European Union

Item Number	Description	Format
10015993	QMS Everolimus Immunoassay*	R1 22 mL, R2 8 mL
373860	QMS Everolimus Calibrator Set*	6 levels, 3 mL 1 vial each
373878	QMS Everolimus Control Set*	3 levels 3 mL 1 vial each

* not available in US

Thermo Scientific QMS
Tacrolimus Immunoassay

Accurate: Correlates well with the gold standard LC-MS/MS methods

Efficient: Quick turn-around of patient results

Convenient: liquid, ready-to-use reagents

Limit of Quantitation: (LOQ): 0.9 ng/mL

Reportable Range: 1.0 – 30.0 ng/mL

Precision

Precision was evaluated using whole blood pooled patient and spiked samples. The study was conducted as described in CLSI protocol EP5-A3.[1] 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.

			Within-Run		Total-Run	
Sample	**N**	**Mean (ng/mL)**	**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

Reference Method Comparison

Correlation studies were performed to compare the QMS Tacrolimus Immunoassay on the Beckman Coulter™ AU680 analyzer to the LC-MS/MS method. The results of the Deming regression analysis using the different transplant type samples are shown in the table below.

Transplant Type	**Number**	**Slope**	**Intercept**	**Correlation**
Kidney	136	1.077	0.98	0.980
Liver	133	1.127	0.21	0.963
Heart	114	1.108	0.36	0.974

Deming regression analysis result with all transplant patient samples are shown in the table below.

Comparative Method	**N**	**Slope (95% CI*)**	**Intercept (95% CI)**	**Correlation Coefficient (R)**
LC-MS/MS System 1	383	1.11 (1.08 to 1.14)	0.53 (0.31 to 0.76)	0.972

*Confidence Interval (CI)

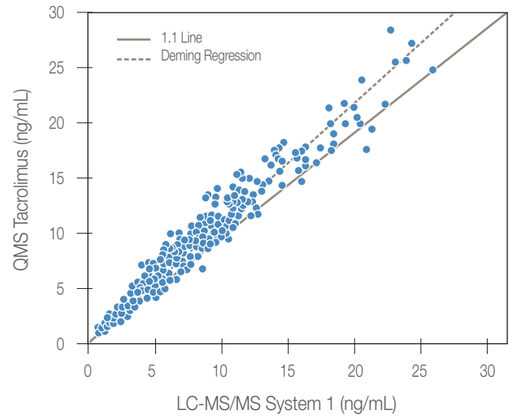
1.) CLSI. Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition. CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014

Ordering:

Item Number	**Description**	**Format**
10015556	QMS Tacrolimus Immunoassay	R1 18 mL, R2 12 mL, Extraction Reagent 50 mL
10015573	QMS Tacrolimus Calibrator Set Level A Level B-F	6 levels 4 mL, 1 vial 2 mL, 1 vial each
280-1	Rap/Tac/CsA Control Level 1	4 mL, 4 vials
280-2	Rap/Tac/CsA Control Level 2	4 mL, 4 vials
280-3	Rap/Tac/CsA Control Level 3	4 mL, 4 vials

Method Comparison

Correlation studies were performed to compare the QMS Tacrolimus Immunoassay to LC-MS/MS System 1. The studies used 383 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[2] between the two methods are shown in the table below.



2.) Deming WE. Statistical adjustment of data. New York: Wiley, 1943. (Dover Publications edition, 1985; Dover Publications, New York)

Thermo Scientific™ CEDIA™
Cyclosporine PLUS Assay

Accurate: Lot-to-lot consistency

Efficient: Two-point calibration curve

Convenient: High and low range assays use same reagents

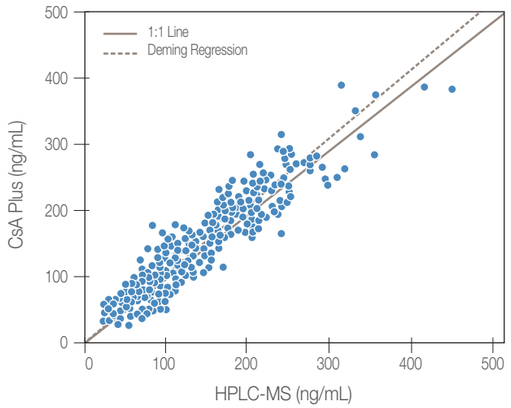
Rapid: Single-lysing step for sample preparation

Limit of Quantitation (LOQ): Limit of Quantitation is 25 ng/mL

Reportable Range: 25 to 2000 ng/mL

Method Comparison - Low Range Assay

Comparisons using Microgenics CEDIA Cyclosporine PLUS (y) to HPLC-MS (x) at four sites provided following correlation on all transplant types.



Reference Method Comparison

Comparisons using Microgenics CEDIA Cyclosporine PLUS (y) to FPIA (x), EMIT® (x), and HPLC-MS (x) at four sites provided the following correlations. Refer to package insert for additional information on method comparison.

Transplant Type	x-Axis	Linear Regression S_{yx}	Deming S_{yx}	R	n	Range
All	HPLC-MS	0.97x + 8 26	1.04x - 1 18	0.93	311	25 – 386 ng/mL
All	EMIT	1.05x + 6 16	1.09x + 2 11	0.97	298	33 – 412 ng/mL
All	Axsym	1.00x + 2 19	1.05x - 5 13	0.95	296	35 – 368 ng/mL
All	TDx	0.87x - 18 20	0.91x - 25 15	0.95	298	9 – 386 ng/mL
Heart/Lung	HPLC-MS	0.87x + 32 26	0.93x + 23 19	0.94	109	31 – 383 ng/mL
Liver	HPLC-MS	1.07x - 0 21	1.18x - 9 13	0.91	80	41 – 386 ng/mL
Kidney	HPLC-MS	1.02x - 9 24	1.09x - 17 16	0.94	122	26 – 379 ng/mL

Precision

Measured precision studies using packaged reagents, pooled whole blood, and whole blood controls yielded the following results in ng/mL on the Hitachi 911 analyzer. The study was conducted using CLSI modified replication experiment (3 replicates, daily for 21 days).

Low Range Assay

	n	Mean	Within Run SD	Within Run CV%	Total SD	Total CV%
Control Level 1	63	46.2	3.7	8.0	7.4	16.0
Control Level 2	63	199.7	5.9	2.9	9.1	4.6
Control Level 3	63	418	31.7	7.6	40.5	9.6
Low Pool	63	54	4.7	8.8	6.6	12.2
High Pool	63	434.7	6.7	1.6	19.4	4.5

High Range Assay

	n	Mean	Within Run SD	Within Run CV%	Total SD	Total CV%
Control Level 4	63	642	38.0	5.9	47.0	7.3
Control Level 5	63	1257	49.9	4.0	63.9	5.1
Low Pool	63	472	22.8	4.8	35.1	7.5
High Pool	63	1695	39.2	2.3	87.3	5.2

Ordering:

Item Number	Description	Format
10016283	CEDIA Cyclosporine PLUS Assay includes Low Range Calibrators A & B	R1 41mL, R2 19 mL, lysing reagent 98 mL, Cal A & B - 2 mL, 1 vial each
100012	CEDIA Cyclosporine PLUS High Range Calibrator Kit	2 levels, 4 mL 2 vials each
280-1	Rap/Tac/CsA Control Level 1	4 mL, 4 vials
280-2	Rap/Tac/CsA Control Level 2	4 mL, 4 vials
280-3	Rap/Tac/CsA Control Level 3	4 mL, 4 vials

Thermo Scientific CEDIA
Mycophenolic Acid (MPA) Assay

Accurate: Correlates well with gold standard method LC-MS/MS

Efficient: Two-point linear calibration

Rapid: No extraction step

Limit Of Quantitation (LOQ): 0.3 µg/mL

Reportable Range: 0.3 to 10 µg/mL

Precision

Control samples were tested in replicates of 2, twice per day for 20 days, yeilding a total of 80 replicates.

		Within-Run		Total	
Sample	**Mean (µg/mL)**	**SD (µg/mL)**	**%CV**	**SD (µg/mL)**	**%CV**
Control 1	0.88	0.05	5.10	0.07	8.10
Control 2	2.84	0.06	1.90	0.08	2.90
Control 3	6.55	0.11	1.70	0.19	2.90

Ordering:

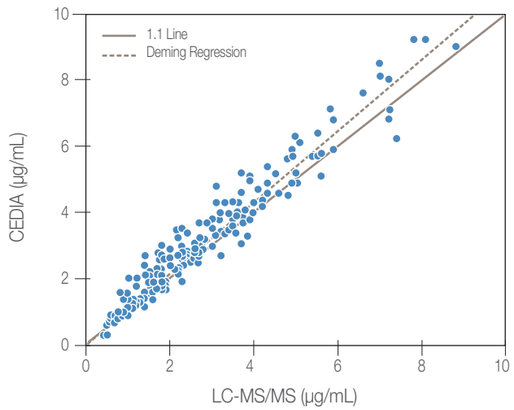
Item Number	Description	Format
10016265	CEDIA Mycophenolic Acid Assay	R1 26 mL, R2 11 mL
100277	CEDIA Mycophenolic Acid Calibrator Set	2 levels, 5.0 mL 2 vials each
100278	MAS™ Mycophenolic Acid Control 1 Kit	1 level, 5.0 mL 4 vials each
100279	MAS Mycophenolic Acid Control 2 Kit	1 level, 5.0 mL 4 vials each
100280	MAS Mycophenolic Acid Control 3 Kit	1 level, 5.0 mL 4 vials each

Method Comparison

A total of 188 pre-dose samples from adult transplant patients receiving mycophenolate mofetil or mycophenolate sodium therapy were tested in a method comparison study using LC-MS/MS as the reference method. The table below summarizes the results of the study with separate analysis by transplant type and combined results.

Sample	N	Regression Method		R
Plasma Heart	96	Least Square slope	1.11 (1.06 to 1.17)	0.97
		Least Square intercept	0.20 (0.05 to 0.36)	
		Deming slope	1.15 (1.09 to 1.20)	
		Deming intercept	0.12 (-0.04 to 0.28)	
Plasma Kidney	92	Least Square slope	1.13 (0.97 to 1.08)	0.97
		Least Square intercept	0.16 (-0.03 to 0.36)	
		Deming slope	1.06 (1.01 to 1.11)	
		Deming intercept	0.06 (-0.13 to 0.25)	
Plasma All	188	Least Square slope	1.05 (1.02 to 1.09)	0.97
		Least Square intercept	0.22 (0.09 to 0.34)	
		Deming slope	1.09 (1.05 to 1.13)	
		Deming intercept	0.12 (-0.01 to 0.25)	

Deming Regression Analysis: Slope was 1.09, and intercept was 0.12 with a correlation coefficient of 0.97.



IMMUNOSUPPRESSANT DRUG TESTING

Thermo Scientific CEDIA
Immunosuppressant drug testing

One of the most effective therapies for patients with end-stage organ failure is solid organ transplantation. Typically, one or more immunosuppressive drugs (ISD) are used to prevent rejection of transplanted organs and tissues. Drug concentrations are periodically measured, which allow physicians to make adjustments to patient's drug therapy, ensuring long-term success by drug monitoring. Immunosuppressant drug monitoring can be done by several methods; the most common method is immunoassay.

We offer a comprehensive menu of Immunosuppressant Drug Management assays, which are recognized worldwide for their ease-of-use, quality, performance, and lot-to-lot consistency.

- **Full ISD menu on a single analyzer**
- **Convenient on-site testing**
- **Improved laboratory efficiency and turnaround time**

Description	Sample Type
CEDIA Cyclosporine PLUS Assay	Whole blood
QMS Tacrolimus Immunoassay	Whole blood
CEDIA Mycophenolic Acid Assay	Plasma
QMS Everolimus Immunoassay	Whole blood

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