Thermo Scientific QMS Everolimus Immunoassay

- Accurate: Correlates well with gold standards and provides excellent accuracy across the assay range
- Convenient: Reagents are liquid, ready to use
- Rapid: Quick turn-around-time
- Limit of Quantitation (LOQ): 2 ng/mL
- Reportable Range: 2 to 20 ng/mL

Newest Generation in Immunosuppressant Testing

Everolimus is an immunosuppressant used to prevent organ rejection in kidney and liver transplants and in selected countries outside of the US, heart transplants. Thermo Scientific™ QMS™ Everolimus Immunoassay uses our proprietary QMS technology, which provides liquid, ready-to-use reagents and excellent accuracy and precision across the assay range. Applications are available on our compact Indiko™ and Indiko Plus clinical and specialty chemistry systems as well as a wide variety of other laboratory instrumentation.

Everolimus acts as a proliferation inhibitor. It inhibits the T cell response to growth factors preventing clonal expansion of activated T cells by inhibiting G1 to S phase. Calcineurin inhibitors, such as cyclosporine and tacrolimus, prevent the activation of T cells by inhibiting G0 and G1. The different modes of action for everolimus and calcineurin inhibitors provide adequate rationale for the pharmacodynamic synergy[1,2].

Monitoring blood everolimus concentrations is recommended as an aid in patient management. Whole blood is the preferred sample matrix because the compound is predominately partitioned in the red cells. Sample must be extracted from the red cells in order to be assayed.

1. Nashan B. The role of Certican (Everolimus, Rad) in the many pathways of chronic rejection. Transplant Proc 2001; 33:3215-3220.

2. Kovarik JM, Kaplan B, Silva HT, etal. Exposure-response relationships for everolimus in de novo kidney transplantation: defining a therapeutic range. Transplantation 2002; 73 (6): 920-925.

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Overview of technology

The Thermo Scientific™ QMS™ Everolimus 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 everolimus antibody reagent. The everolimus-coated microparticle reagent is rapidly agglutinated in the presence of the anti-everolimus 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 everolimus 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 everolimus concentration and the lowest agglutination rate at the highest everolimus concentration.

Precision: **Precision was determined as described in CLSI protocol EP5-A2.12**

A tri-level human blood based control containing everolimus and a tri-level patient sample pool was used in the study. Each level 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 and the within run, between run, between day and total CV were calculated. Representative results are shown below.

20-Day Precision Study: Kidney Transplant Patient Samples

Sample	Expected Values (ng/mL)	Total N	Mean (ng/mL)	Within Run %CV	Between Run %CV	Between Day %CV	Total %CV
Control Level 1	4.0	80	4.1	3.9	2.8	2.7	5.6
Control Level 2	8.0	80	8.1	3.8	2.6	3.4	5.7
Control Level 3	15.0	80	16.3	3.6	3.4	3.7	6.2
Patient Pool 1	2.9	80	2.8	5.6	4.8	4.5	8.6
Patient Pool 2	6.0	80	5.8	2.3	3.6	1.9	4.7
Patient Pool 3	10.5	80	10.1	2.4	2.1	2.8	4.2

Method Comparison Regression Analysis with Kidney Transplant Patient Samples

A correlation study was performed using 124 trough samples from adult kidney transplant patients in the everolimus drug trial. Results from the QMS Everolimus assay were compared with results from two LC-MS/MS methods (System 1 and System 2). The LC-MS/MS System 1 was used in the everolimus drug trial. LC-MS/MS System 2 is used in QMS Everolimus calibrator value assignment. Results of the Passing-Bablok analysis for this study are shown below[3].

		Passing-Bablok		
Comparative Method	N	Slope 95% CI	Intercept 95% CI	Correlation R
QMS vs. LC-MS/MS System 1	124	0.92 (0.87 to 0.98)	0.17 (-0.15 to 0.54)	0.94
QMS vs. LC-MS/MS System 2	124	1.01 (0.95 to 1.08)	-0.15 (-0.50 to 0.17)	0.95

Method Comparison Regression Analysis with Liver Transplant Patient Samples

A correlation study was performed using 178 samples from adult liver transplant recipients, where the majority of patients were co-administered tacrolimus. The samples were collected from this population pre-dose (except for some of the samples at the assay upper limit), at a time post-transplant mostly ranging from 9 to 26 months. Results from the QMS Everolimus Immunoassay were compared with results from two LC-MS/MS methods; both methods were used in the everolimus drug trial for liver transplantation. Two lots of reagents were used to measure liver transplant patient samples by QMS Everolimus Immunoassay. Results of the Passing-Bablok analysis for this study are shown below.

		Passing-Bablok		
Comparative Method	N	Slope 95% CI	Intercept 95% CI	Correlation R
QMS (Rgt lot 1) vs. LC-MS/MS System 1	178	1.07 (1.03 to 1.12)	0.07 (-0.22 to 0.33)	0.96
QMS (Rgt lot 2) vs. LC-MS/MS System 1	178	1.04 (1.01 to 1.09)	-0.22 (-0.41 to 0.01)	0.97
QMS (Rgt lot 1) vs. LC-MS/MS System 3	178	1.07 (1.02 to 1.13)	0.19 (-0.14 to 0.43)	0.97
QMS (Rgt lot 2) vs. LC-MS/MS System 3	178	1.06 (1.02 to 1.10)	-0.09 (-0.32 to 0.10)	0.97

Method Comparison Regression Analysis with Heart Transplant Patient Samples

		Passing-Bablok		
Comparative Method	N	Slope 95% CI	Intercept 95% CI	Correlation R
QMS vs. LC-MS/MS	41	1.00 (0.89 to 1.16)	-0.15 (-1.02 to 0.65)	0.96

Rely on the Thermo Scientific QMS Everolimus Immunoassay results for the crucial monitoring of everolimus drug levels in kidney and liver transplant patients within in the US and heart transplants in other selected countries. Using our proprietary QMS technology, these liquid, ready-to-use reagents provide excellent accuracy and precision. Applications are available on our compact Thermo Scientific™ Indiko™ and Indiko Plus clinical and specialty chemistry systems as well as a wide variety of other laboratory instrumentation.

3. Bablok W, Passing H, Bender R, Schneider B. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry. Part III J Clin Chem Clin Biochem 1988; 26 (11): 783-790.

Ordering Information

For Use in the USA Only			
Part Number	**Description**	**Format**	**Storage and Shelf-Life**
10015987*	QMS Everolimus Immunoassay for the Indiko	R1 - 1 x 22 mL, R2 - 1 x 8 mL, Precipitation Rgt 1 x 8 mL	2 to 8 °C until expiration date on the kit
0380000	QMS Everolimus Immunoassay	R1 - 1 x 22 mL, R2 - 1 x 8 mL, Precipitation Rgt 1 x 8 mL	
0380005	QMS Everolimus Calibrator Set	6 Levels, 1 x 3 mL	-20 ± 5 °C until expiration date on the kit, 2 to 8 °C for 6 weeks after thawing.
0380010	QMS Everolimus Control Set	3 Levels, 1 x 3 mL	

For International Use Only			
Part Number	**Description**	**Format**	**Storage and Shelf-Life**
10015993*	QMS Everolimus Immunoassay for the Indiko	R1 - 1 x 22 mL, R2 - 1 x 8 mL, Precipitation Rgt 1 x 8 mL	2 to 8 °C until expiration date on the kit
0373852	QMS Everolimus Immunoassay	R1 - 1 x 22 mL, R2 - 1 x 8 mL, Precipitation Rgt 1 x 8 mL	
0373860	QMS Everolimus Calibrator Set	6 Levels, 1 x 3 mL	-20 ± 5 °C until expiration date on the kit, 2 to 8 °C for 6 weeks after thawing.
0373878	QMS Everolimus Control Set	3 Levels, 1 x 3 mL	

*Indiko reagent kits contain bar-coded bottles. They use the same calibrators and controls.

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