Performance of the Everolimus Assay on the Dimension Clinical Chemistry Systems

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Introduction

Immunosuppression is important for successful organ transplantation to help prevent organ rejection. While each immunosuppressant drug (ISD) has its own mechanism of action, the goal is always the same: to provide adequate immunosuppression so that transplanted organs are not rejected by a recipient's immune system.

To accomplish this, clinicians must work carefully to reach an appropriate level of immunosuppression while minimizing the toxic side effects that these drugs have on the patient. Common side effects associated with ISD therapy include nephrotoxicity, neurotoxicity, glucose intolerance, diarrhea, and neoplasm. There are several immunosuppressant drugs available to help support transplant management, classified according to their mechanism of action. Cyclosporine, tacrolimus, mycophenolate mofetil (MMF), everolimus, and sirolimus are currently the most frequently prescribed ISDs.[1]

The Dimension® Everolimus assay is for in vitro diagnostic use in the quantitative measurement of everolimus in human whole blood (EDTA) using the Dimension® Clinical Chemistry Systems. The Dimension Everolimus assay is intended for use as an aid in the management of everolimus therapy in kidney, liver, and heart transplant patients.[2]

Assay specifications[2]

Parameter	Description
Assay principle	Affinity chrome mediated immunoassay (ACMIA)
Sample type	Whole blood
Sample pretreatment	No manual pretreatment by user; performed automatically onboard instrument
Sample volume	12 µL
Measuring interval	1.0–25.0 ng/mL (1.0–26.1 nmol/L)
Reagent shelf life	2–8°C until expiration date on product
Reagent onboard stability	30 days
Reagent open stability	2 days
Turnaround time (TAT)	19 minutes
Calibration interval	30 days
Limit of quantitation (LOQ)	1.0 ng/mL (1.0 nmol/L)
Limit of detection (LOD)	0.6 ng/mL (0.6 nmol/L)
Limit of blank (LOB)	0.1 ng/mL (0.1 nmol/L)
Dilutions	Manual, not to exceed dilution factor of 2

Precision[2]

Precision was determined in accordance with CLSI document EP05-A3. Six samples were assayed on the Dimension Clinical Chemistry System in duplicate in two runs per day for 20 days.

		Repeatability		Within-Laboratory	
Material	Mean	SD	%CV	SD	%CV
QC1	2.0 ng/mL (2.1 nmol/L)	0.06	3.0	0.09	4.8
QC2	5.4 ng/mL (5.6 nmol/L)	0.09	1.7	0.23	4.2
QC3	11.6 ng/mL (12.1 nmol/L)	0.25	2.2	0.65	5.6
Patient Pool 1	3.1 ng/mL (3.2 nmol/L)	0.05	1.7	0.15	4.8
Patient Pool 2	7.4 ng/mL (7.7 nmol/L)	0.13	1.7	0.35	4.8
Patient Pool 3	14.2 ng/mL (14.8 nmol/L)	0.29	2.0	0.97	6.9

Ready to Use

No Manual Prep
No Standing Time

Our liquid, ready-to-use Dimension assays streamline operations, with no manual sample pretreatment or standing time before use.

Liquid, ready-to-use reagents and calibrators with extended calibration stability mean less hands-on time for operators and greater efficiency.

Workflow with Dimension ISD testing

When performing ISD tests on whole blood samples in the laboratory, the most time-consuming step in the workflow is preparing the sample for testing on the analyzer. For accurate measurement, the drug must be extracted from inside the red blood cells via a pretreatment process. Each manufacturer provides the diluents and reagents required to perform each step of the pretreatment process for their assay and instrument. This sample pretreatment takes time, requires training for laboratory staff, and is at risk for human error. In addition, because of the manual nature of this step, testing is often performed in batches to maximize efficiency of the technologist and instrument.

On the Dimension Clinical Chemistry System, the entire pretreatment process is automated. The instrument receives the whole-blood sample and performs the sample pretreatment onboard, completely eliminating hands-on time for laboratory staff, risk of human error, and the need for batch testing.

Physicians who are establishing dosing for post-transplant patients, checking peak-trough for existing patients, or working through an urgent dosing issue can obtain immediate results without the cost of sending out or waiting on the laboratory's next batch schedule.

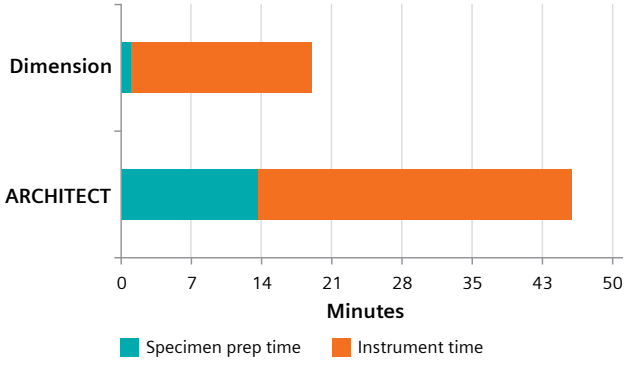
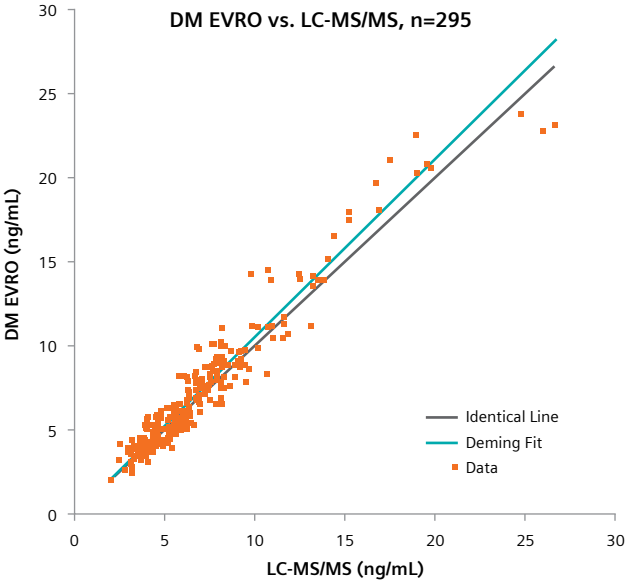


Figure 1. Dimension and ARCHITECT Systems—average processing time per sample.

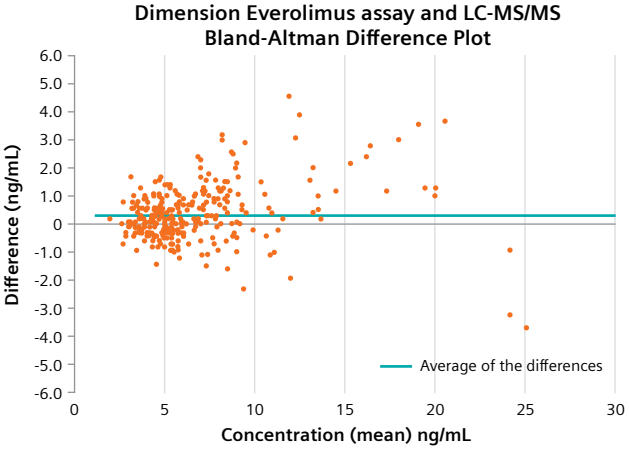
Method comparison to LC-MS/MS (reference)[3]

Method comparison was performed based upon CLSI document EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples. A total of 295 whole blood samples (varied from heart, liver, and kidney transplant patients) were aliquoted and stored at –70°C. All samples were tested with two Flex® lots on the Dimension® EXL™ 200 Integrated Chemistry System. The EVRO sample values ranged from 2.0 to 26.7 ng/mL. A second aliquot of each of the 295 samples was tested for everolimus by LC-MS/MS.

Comparative Method	Slope (95% CI)	Intercept ng/mL (95% CI)	Correlation Coefficient	n
LC-MS/MS	1.06 (0.98–1.14)	–0.10 (–0.59 to 0.39)	0.965	295



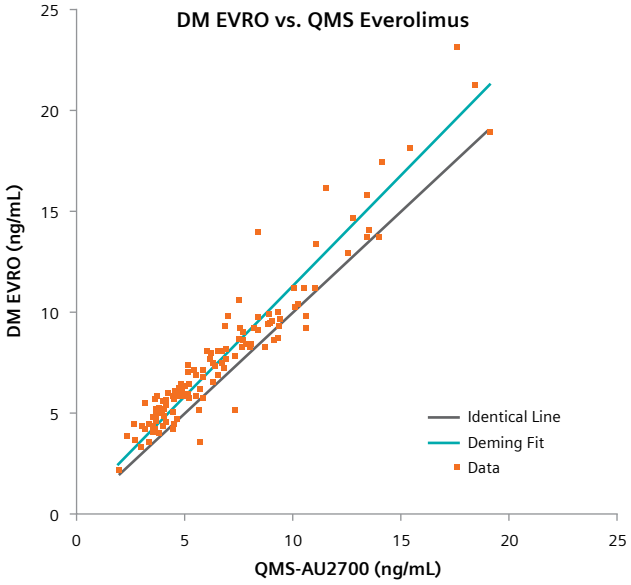
A Bland-Altman analysis of the Dimension Everolimus assay and LC-MS/MS results is shown below. The average bias between the Everolimus assay and LC-MS/MS method was 0.3 ng/mL (0.3 nmol/L).



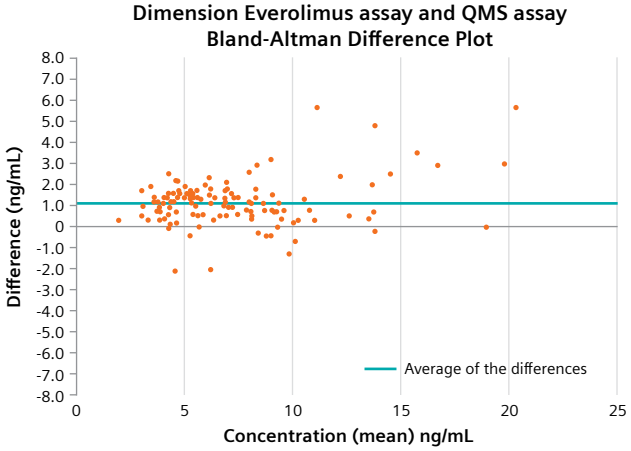
Method comparison to QMS Everolimus assay on Beckman AU2700 system (predicate)[3]

Method comparison testing was performed based upon CLSI document EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples. A total of 125 whole blood samples (varied heart, liver, and kidney transplant patients) were aliquoted and stored at –70°C. All samples were tested with one lot of the Thermo Scientific QMS Everolimus assay (predicate) on the AU2700 system and one Dimension Everolimus Flex lot on the Dimension EXL 200 Integrated Chemistry System. The sample values ranged from 1.9 to 19.1 ng/mL due to the QMS Everolimus assay range of 1–20 ng/mL.

Comparative Method	Slope (95% CI)	Intercept ng/mL (95% CI)	Correlation Coefficient	n
QMS Everolimus	1.09 (0.99–1.19)	0.44 (–0.18 to 1.05)	0.954	125



A Bland-Altman analysis of the Dimension Everolimus and QMS assay results is shown below. The average bias was 1.1 ng/mL (1.1 nmol/L).



Summary

The Dimension Everolimus (EVRO) assay on Dimension Clinical Chemistry Systems provides laboratories with an improved workflow with no manual pretreatment and trusted results that align with the LC-MS/MS reference method. Physicians have 24/7 access to important patient results in less than 20 minutes as well as a full ISD testing menu including cyclosporine, mycophenolic acid, sirolimus, and tacrolimus—all on one easy-to-use system.

Transplant medicine depends on reliable results. At Siemens Healthineers, we value the trust of our physicians and laboratories and are committed to providing comprehensive, high-quality testing solutions for transplant patients around the world.

References:

1. Van Sandwijk, et al. Immunosuppressive drugs after solid organ transplantation. The Journal of Medicine. 2013 Jul/Aug;71(6).
2. Dimension Everolimus Assay Instructions for Use (IFU) 11417409_ EN Rev. 01, 2021-05.
3. Dimension Everolimus Design Verification Report, Version: 8.0.
4. Reducing manual steps, improving turnaround times, and creating a lean laboratory environment: ISD testing on the Dimension® Integrated Chemistry Systems.

Ordering information

Product	Part No.	SMN	Contents
Dimension EVRO Reagent Cartridge	DF307	11318969	80 tests (4 Flex cartridges x 20 tests each)
Dimension EVRO Cal (5 levels)	DC307	11318970	Level 1: 2 x 2 mL vials Levels 2–5: 2 x 1 mL vials
Ev/Tac/CsA Control LV1	305-1	11554030	Level 1: 6 x 4 mL vials
Ev/Tac/CsA Control LV2	305-2	11554031	Level 2: 6 x 4 mL vials
Ev/Tac/CsA Control LV3	305-3	11554032	Level 3: 6 x 4 mL vials
Ev/Tac/CsA Control LV 1, 2, 3	305	11554033	Level 1–3: 2 x 4 mL vials

Verification studies were performed on the Dimension EXL 200 system. Additional studies were performed on Dimension RxL, Xpand®, and/or EXL w/LM Systems. All systems used Dimension software version 10.3 or higher.

At Siemens Healthineers, our purpose is to enable healthcare providers to increase value by empowering them on their journey toward expanding precision medicine, transforming care delivery, and improving patient experience, all made possible by digitalizing healthcare.

An estimated 5 million patients globally benefit every day from our innovative technologies and services in the areas of diagnostic and therapeutic imaging, laboratory diagnostics, and molecular medicine, as well as digital health and enterprise services.

We are a leading medical technology company with over 120 years of experience and 18,000 patents globally. Through the dedication of more than 50,000 colleagues in 75 countries, we will continue to innovate and shape the future of healthcare.

Product availability may vary from country to country and is subject to varying regulatory requirements. Please contact your local representative for availability.

Siemens Healthineers Headquarters
Siemens Healthcare GmbH
Henkestr. 127
91052 Erlangen, Germany
Phone: +49 9131 84-0
siemens-healthineers.com

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Siemens Healthcare Diagnostics Inc.
Laboratory Diagnostics
511 Benedict Avenue
Tarrytown, NY 10591-5005
USA
Phone: +1 914-631-8000

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