

Metrological Traceability of the Waters™ MassTrak™ Immunosuppressant Calibrator and Quality Control Sets

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This is an Application Brief and does not contain a detailed Experimental section.

For *in vitro* diagnostic use. Not available in all countries.

Abstract

Within clinical laboratories, there is a requirement to follow local regulatory guidelines and international standards when developing and validating laboratory developed tests (LDTs). Furthermore, in some geographies, the implementation of ISO 15189:2012 *Medical laboratories -- Requirements for quality and competence* necessitates that laboratory use metrologically traceable calibration materials. Therefore, metrological traceability and accuracy of results are integral components of the design, development and manufacture of the Waters MassTrak Immunosuppressant Calibrator and Quality Control Sets (IVD), aiding laboratories in the harmonization of their results when using validated LC-MS/MS methods.

In this application brief, we provide an overview of the Waters MassTrak Immunosuppressant Calibrator and Quality Control Sets and their accuracy and comparisons across lot-to-lot testing.

Benefits

- Lyophilized calibrators and quality controls (QC), with established shelf-life and stability data, that reduce sample preparation time
- Confidence in the accuracy of immunosuppressants, measurement of uncertainty and lot-to-lot and provides a path to laboratory method harmonization

Introduction

Clinical laboratories adhere to local regulatory guidelines and international standards such as ISO 15189 that requires the laboratory to demonstrate quality and competence. The manufacture of calibration and QC materials to high standards and quality processes which are metrologically traceable provides a pathway towards laboratory harmonization with minimal variability across different manufacturing lots. LC-MS/MS methods in many clinical laboratories are based on LDTs, which can involve significant manual preparation in the pre-analytical workflow. This can include the preparation and characterization of in-house calibrator and QC materials by the laboratory technician, which may result in errors and inaccuracies of the materials, leading to reductions in lab efficiency.

The Waters MassTrak Immunosuppressant Calibrator and Quality Control Sets (IVD) (Figure 1) contain cyclosporine, everolimus, sirolimus, and tacrolimus in lyophilized human whole blood that have been sourced to obtain the highest level of metrological traceability available. There are no SI traceable reference materials or reference measurement procedures for these immunosuppressants. All immunosuppressant concentrations were confirmed with independent International Proficiency Testing (IPT) scheme samples and secondary reference materials in whole blood (sirolimus and tacrolimus only).



Figure 1. The Waters MassTrak Immunosuppressant Calibrator and Quality Control Sets.

Results and Discussion

Improvements in Laboratory Efficiency

The MassTrak Immunosuppressant Calibrator and Quality Control Sets have been designed and manufactured to increase efficiencies in the pre-analytical workflow by providing ready-to-use (following reconstitution) metrologically traceable calibrator and QC materials. The key benefits, highlighted in Table 1, include the significant time and resource savings made by eliminating the multiple steps a laboratory performs when preparing in-house calibrators. The lyophilized reagents, prepared using well-documented manufacturing and quality processes, demonstrate good lot-to-lot variability and longer shelf-life (up to three years) and in-use

stability (up to 31 days) than traditional in-house reagents.

Preparation of in-house calibrators	MassTrak immunosuppressant calibrator set
Source solid materials	✓
Source matrix	✓
Gravimetric preparation of calibrators	✓
Stability evaluation	✓
Calibrator accuracy evaluation	✓
Lot-to-Lot evaluation	✓
Measurement of uncertainty	✓

Table 1. Improvements in Laboratory Efficiency.

Metrological Traceability and Accuracy

Pursuant to ISO 15189, there are no higher-order reference procedures or reference materials for the immunosuppressants. Therefore, to aid laboratory harmonization, the MassTrak Immunosuppressant Calibrator and Quality Control Sets are confirmed using secondary reference materials (results are shown in Table 2).

ERM summary: % bias from target		
Analyte/ Lot	3519	2517
Sirolimus (ERM-DA111)	-9.3	-4.1
Tacrolimus (ERM-DA110)	-1.3	-2.6

Table 2. Accuracy of ERM reference materials.

Lot-to-Lot Comparisons

The accuracy of the calibrator set was determined through evaluation of in-house QC and IPT samples (spanning the calibration range). Three lots of manufacturing material for the calibrators were evaluated for accuracy by measurement of IPTs using a routine LC-MS/MS measurement procedure. The mean %deviation from the IPT target values as measured by each lot of calibrator material was determined to demonstrate

accuracy (to the harmonized IPT scheme). Results are shown in Figure 2 which not only demonstrates the accuracy of the calibrators but also the lot-to-lot reproducibility of the manufacturing process, which is important if laboratories seek to maintain their harmonization standards overtime using different manufacturing lots.

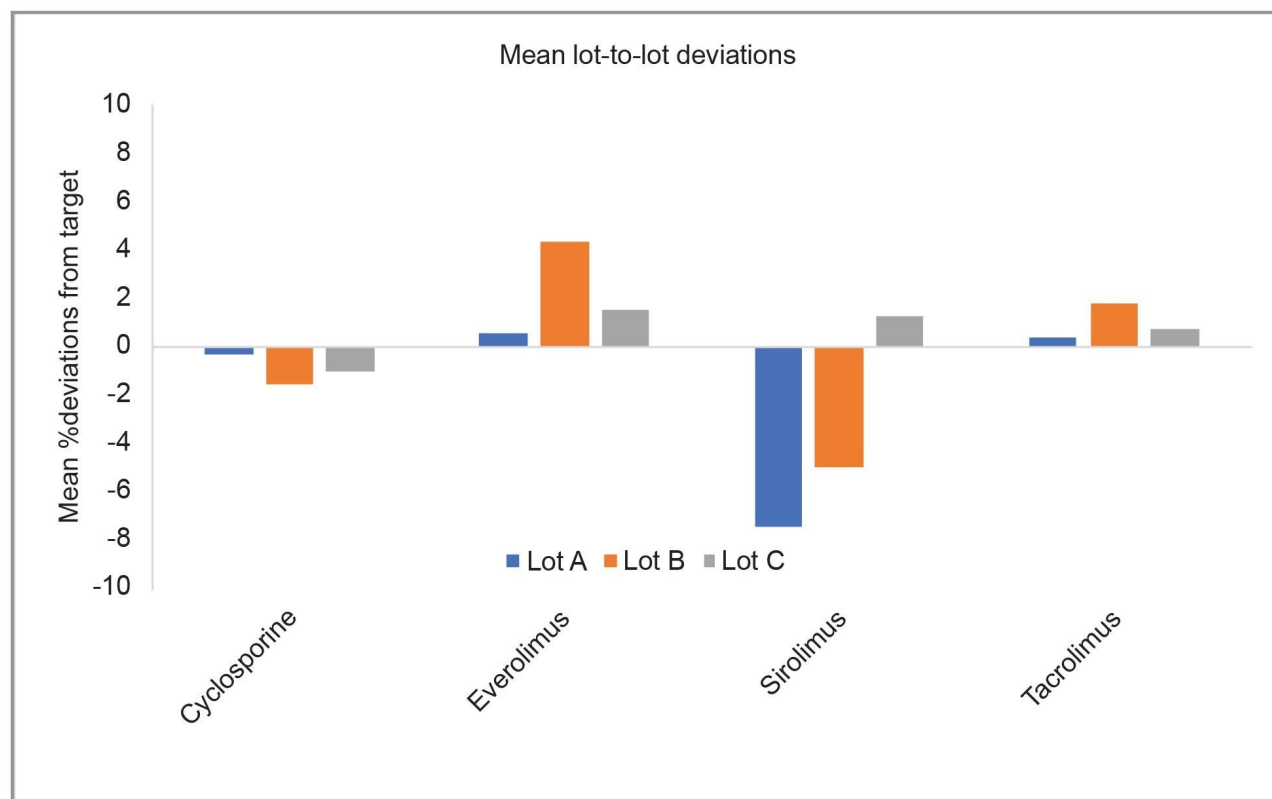


Figure 2. Lot-to-lot comparison of mean % deviations from IPT target values for manufacturing lots A-C for the immunosuppressants demonstrating the accuracy of the MassTrak Immunosuppressant Calibrator Set.

Conclusion

Metrological traceability of the MassTrak Immunosuppressant Calibrator and Quality Control Sets has been established aiding laboratories in their compliance to ISO 15189. The accuracy and lot-to-lot reproducibility have been confirmed through the use of independent international proficiency testing schemes. In addition, the

laboratory workflow has been improved by removing time-consuming, low value tasks, which frees qualified staff for more important tasks.

Disclaimer

MassTrak Immunosuppressant Calibrator and Quality Control Sets are not available for sale in all countries. For information on availability, please contact your local sales representative.

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