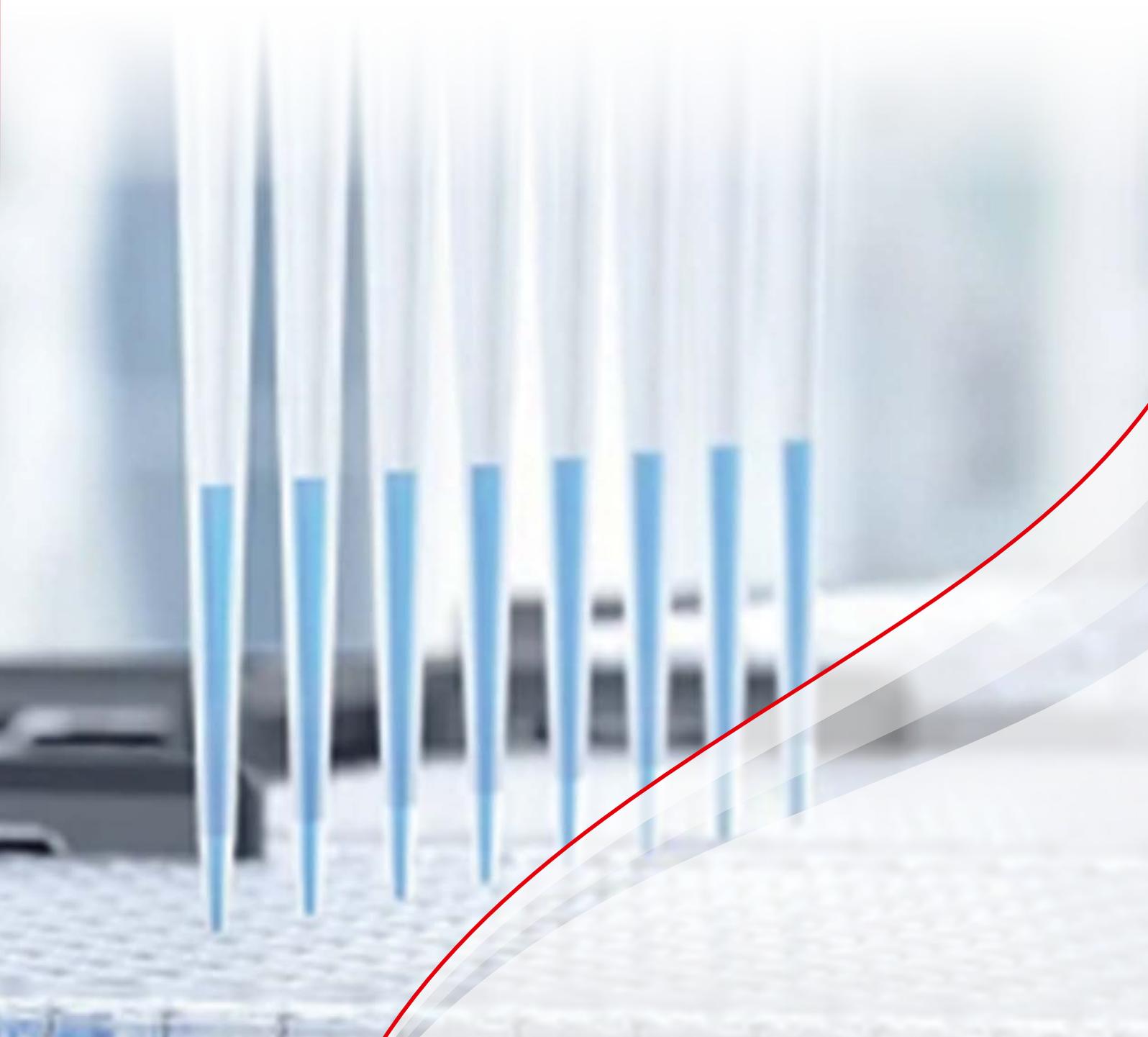


DOSIMMUNE™ with Liquid Handler

The complete IVD solution for immunosuppressant analysis



The DOSIMMUNE kit is a ready-to-use turnkey solution

for simultaneous quantification of four key immunosuppressant drugs in whole blood with:

- Calibrators with 6 levels and blank, internal standards and quality controls with 4 levels
- **Ready-to-use consumables:** Calibrator, Internal standard, Quality Control, Mobile Phase A, Mobile Phase B, System Cleaning Phase, Extraction & Reconstitution Buffer, Analytical & Trap Columns

Ref.	Description
227-40100-55	DOSIMMUNE™ kit for 1,000 analyses (CE-IVD)
227-40101-55	DOSIMMUNE™ kit for 500 analyses (CE-IVD)

Key benefits

Highly reliable – metrological traceability chain

Calibrator and control concentration values provided on the certificate of analysis are obtained from a comparison with certified reference materials and primary standards traceable to the International System of Units (SI) and higher order standards through an unbroken chain of comparisons. The traceability chain and expanded uncertainties are also provided according to ISO 17511.

Easy to set on Liquid Handler*

without transferring to other containers

(*) Example: Hamilton Microlab STAR CL Liquid Handling System (CE-IVD class A device).



High throughput

With automated sample preparation

Stable data

Using Shimadzu LC-40 CL series and LCMS-8050 CL / 8060 CL / 8060NX CL (CE-IVD class A devices)



Methods and documentation

Complete documentation including manual with analytical and sample preparation methods, safety data sheets, certificates of analysis, expiry dates, etc.



Validation results

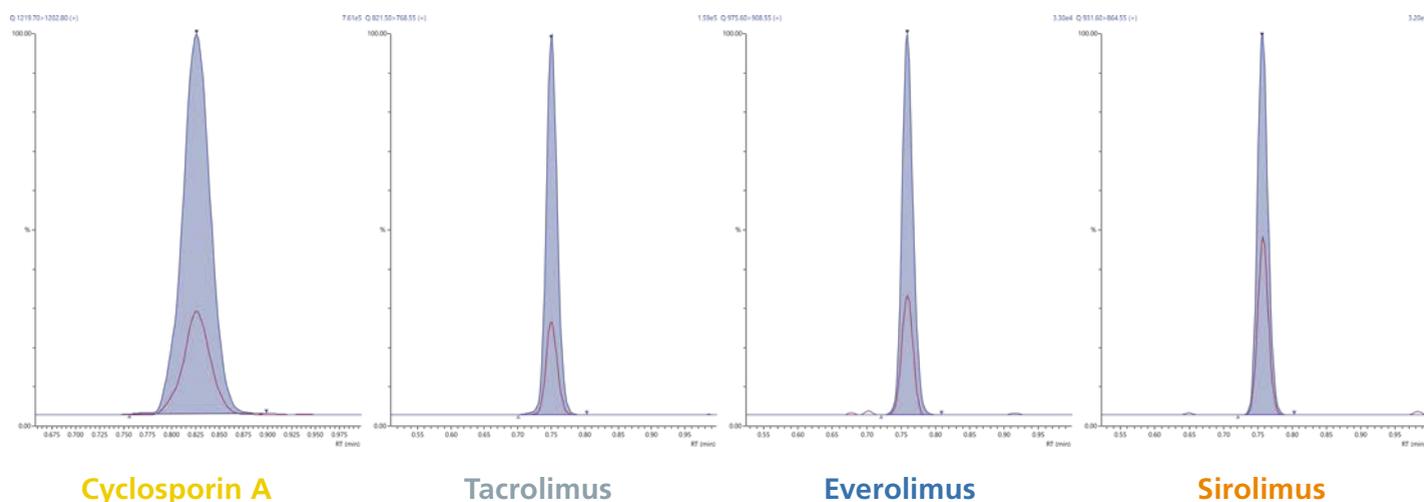
The method, including automated sample preparation, has been fully validated following international bioanalytical guidelines (ICH M10), including from the Clinical and Laboratory Standards Institute (CLSI C62-A).

	Calibrator concentrations (µg/L)	Linearity	Limit of quantification
• Cyclosporin A	25–1,800 µg/L	Up to 3,000 µg/L	≤ 5.0 µg/L
• Tacrolimus	2–35 µg/L	Up to 100 µg/L	≤ 0.5 µg/L
• Everolimus	2–35 µg/L	Up to 100 µg/L	≤ 0.5 µg/L
• Sirolimus	2–35 µg/L	Up to 100 µg/L	≤ 0.5 µg/L

Precision and accuracy	QC1 (low)	QC2 (low-mid)	QC3 (middle)	QC4 (high)
• Cyclosporin A	4.3% 4.6% 105%	3.0% 3.2% 98.6%	2.8% 3.5% 100%	2.2% 2.5% 101%
• Tacrolimus	3.2% 3.2% 89.9%	3.1% 3.7% 97.7%	3.9% 4.5% 96.1%	4.0% 4.1% 103%
• Everolimus	5.9% 6.5% 99.3%	5.1% 6.2% 97.0%	4.7% 4.7% 92.9%	4.5% 5.9% 102%
• Sirolimus	9.2% 9.2% 93.9%	4.6% 4.7% 98.4%	4.8% 4.9% 95.8%	4.8% 5.4% 104%

Intra-assay precision | Inter-assay precision | Accuracy (n = 25, 5 independent series)

Typical chromatograms



High throughput

Automated sample preparation

Sample preparation

45 min per 96 well plate with Liquid Handler* (including all relevant preparation steps up until readiness for LC/MS/MS injection (sampling, ISTD addition, extraction and centrifugation))



(* e.g. Hamilton Microlab STAR CL (CE-IVD class A device) Liquid Handling System)

LC/MS/MS analysis

1.5 min per sample



Shimadzu LC-40 CL series and LCMS-8050 CL / 8060 CL / 8060NX CL (CE-IVD class A devices)

1) 1 x Liquid Handler and 1 x LC/MS/MS

- Delivers more than 120 real sample results within hours
- Capable of analyzing more than 200 samples in approx. 7 hours

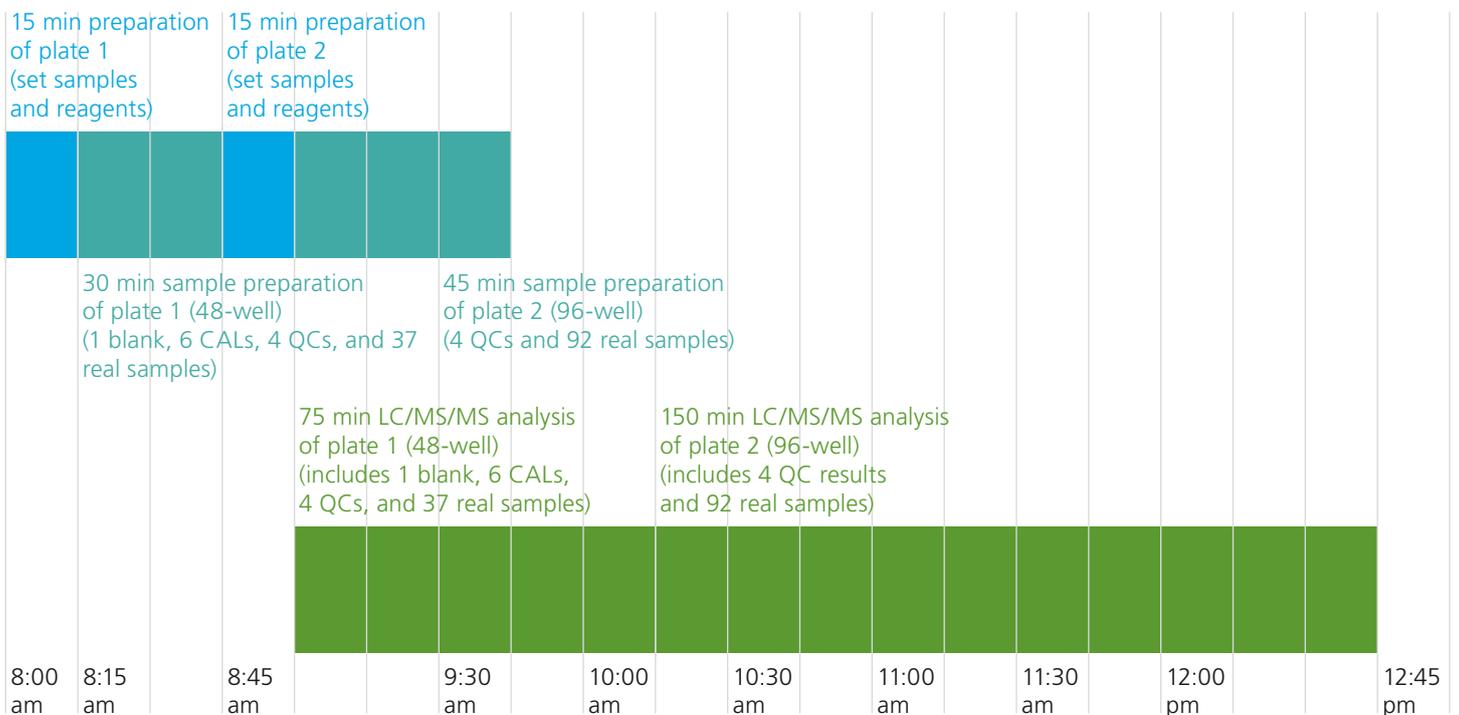


Figure 1: Example workflow with 1 x Liquid Handler and 1 x LC/MS/MS

2) 1 x Liquid Handler and 2 x LC/MS/MS

- Delivers more than 160 real sample results within hours
- Capable of analyzing more than 340 samples in approx. 7 hours

Stable data

Analysis using Shimadzu LC/MS/MS



The stable isotope-labeled internal standard (ISTD) area values between two calibrations must be stable to ensure accurate quantification.

The ISTD in the DOSIMMUNE kit can be mixed with the extraction buffer, and mixture can be delivered through the Liquid Handler's automated supply unit.

As a result (Figure 2), there is little ISTD area variation for any of the immunosuppressants throughout the three 96-well plates, with a %RSD of less than 5.8 % (n = 278).

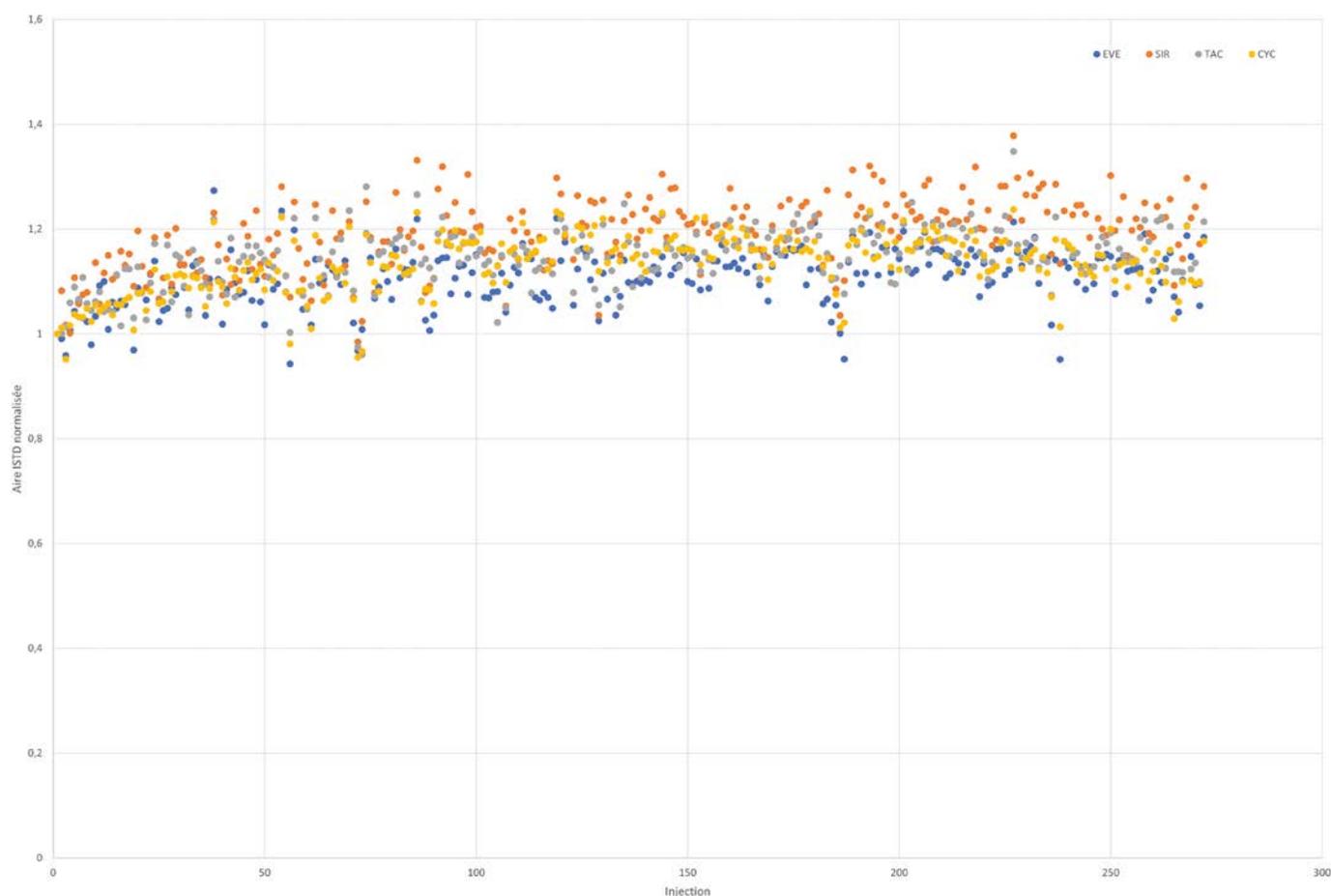


Figure 2: Normalized ISTD area for QC samples pretreated with Hamilton Microlab STAR (n = 278, for 3 96-well plates)

Manufactured by:

ALSACHIM

a Shimadzu Group Company

 **Alsachim**

Parc d'innovation - Les Scientifiques

160 rue Tobias Stimmer

67400 Illkirch-Graffenstaden

France

www.alsachim.com

Distributed by:

 **SHIMADZU**

Shimadzu Europa GmbH

Albert-Hahn-Str. 6–10

D-47269 Duisburg

Tel.: +49 (0) 203 7687 0

Fax: +49 (0) 203 7666 25

ALC-Kits@shimadzu.eu

www.shimadzu.eu

These devices are only available in markets where the conformity assessment procedure of the product (CE IVDR) is accepted.

Shimadzu is placing DOSIMMUNE on the market in accordance with the European Regulation for in vitro diagnostic medical devices (IVDR 2017/746).

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