

## Reducing your chance of rejection

LGC scientists contribute to reducing the likelihood of organ rejection by developing reference methods and materials to support therapeutic drug monitoring and sharing their measurement expertise with front-line hospital laboratories to help them provide better patient care.



Department for  
Business, Energy  
& Industrial Strategy

## The requirement

Organ transplantation allows people with organ failure the opportunity to resume a normal life through the receipt of a suitable organ from a donor. To ensure the approximately 4,500 organ transplants carried out each year remain viable, a complex regimen of drugs (immunosuppressants) is required to prevent the patient rejecting the donor organ.

Whilst life-saving at the right doses, immunosuppressant drugs have a very narrow therapeutic range and too much can be toxic, potentially causing diabetes, skin cancer or even resulting in kidney failure, leading to a need for dialysis or further organ donation. Consequently, the therapeutic levels of immunosuppressants in the blood of each patient must be accurately measured by healthcare workers.

There has been significant variation in measurement results for immunosuppressants shown across different methods and between different hospital laboratories, demonstrating the clinical need for these measurements to be standardised.

Through the recent implementation of the new ISO Standard 15189 in the UK the demonstration of standardisation is now a requirement for hospital laboratories. This requires the provision of fully validated methods and certified reference materials for clinical analytes such as immunosuppressants.

## The solution

Scientists at LGC have developed higher order reference materials for the two most commonly prescribed immunosuppressants: tacrolimus (ERM-AC022, ERM-DA110) and sirolimus (ERM-AC021a, ERM-DA111a), under LGC's accreditation to ISO Guide 34 as a Reference Material Producer.

The values for the materials have been assigned using fully validated high accuracy reference methods with complete uncertainty assessments and, in the case of the whole blood materials, demonstration of commutability<sup>a</sup>. Two of the materials (ERM-DA110, ERM-AC021a) have been included in the Joint Committee for Traceability in Laboratory Medicine (JCTLM) database of higher order reference materials.

In addition to the production of these materials, LGC scientists have used the developed methods to supply target reference values to samples used for external quality assurance (EQA) schemes and in the validation of in vitro diagnostic (IVD) kits for manufacturers.

## The impact

By 2017 the NHS is dedicated to increasing organ transplantation rates by 60%. Supported by accurate measurement of immunosuppressant levels to reduce organ rejection rates, this could achieve costs saving of £200 million per year through, for example, savings of dialysis costs.

Beyond the financial implications, a well-controlled therapeutic drug monitoring regime (TDM) can mean the difference between life and death for some organ transplant patients. Accurate measurements for TDM give patients the best possible chance of an improved quality of life, away from hospital beds and dialysis machines.

Our immunosuppressant reference materials are being used by the world's leading in vitro diagnostics companies as well as secondary standard producers such as RECIPE (ClinCal® Whole Blood Calibrators for Immunosuppressants) and ChromSystems (MassCheck® Immunosuppressants Whole Blood Controls) to underpin existing or in-development assays.

Furthermore, the expert knowledge gained throughout this work is being shared with those at the front line: the hospital laboratory staff, hospital doctors and measurement equipment manufacturers, to support laboratories working to ISO 15189 and help improve routine clinical measurements.

Professor David Holt, Professor of Bioanalytics at Analytical Services International, University of London

*"Standardised measurement of immunosuppressant drugs presents a major challenge for clinical laboratories and the diagnostics industry. The provision of high accuracy measurement tools, such as those provided by LGC, will help in setting and maintaining optimal patient dosage, which could directly benefit patients and ensure consistent care across transplant centres globally."*

<sup>a</sup> reference T M Annesley, D A McKeown, D W Holt, C Mussell, E Champarnaud, L Harter, L J Calton, D S Mason.  
*Clin Chem* (2013) 59(11)1630-1637

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