Department for Business, Energy & Industrial Strategy

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LGC

# THE NATIONAL MEASUREMENT LABORATORY AND DESIGNATED INSTITUTE FOR CHEMICAL AND BIO-MEASUREMENT

## ANNUAL REVIEW 2016

# LGC AS A DESIGNATED INSTITUTE

LGC delivers underpinning measurement science in our role as the UK National Measurement Laboratory and Designated Institute (DI) for chemical and bio-metrology. As a DI we form part of the UK National Measurement System (NMS), a collaboration of laboratories funded by the UK Government Department for Business, Energy and Industrial Strategy (BEIS) that provides the core measurement infrastructure for the UK.

LGC is established as one of the top institutes world-wide within our scope of designation. As a DI we have two key roles:

- ensuring trust and confidence in chemical and bio-measurements in the UK though our state-of-the-art measurement capabilities, as identified by government strategy and industry needs

- addressing measurement challenges of the future to foster innovation, promoting productivity and economic growth

Our research areas span the sectors of advanced therapeutics, diagnostics and safety & security and are delivered through the four core streams of measurement research, calibration facilities, reference materials, and training and consultancy. Through improved chemical and bio-measurements we support manufacture and trade, protect consumers and enhance skills development and quality of life.

LGC plays a leading role internationally to develop laboratory best practice and harmonise measurements across the world. Our international position provides further confidence in the UK's science and technology capabilities.

# EXECUTIVE SUMMARY

This is our second annual review of LGC's Designated Institute (DI) function as the National Measurement Laboratory for chemical and bio-measurement.

We are extremely proud to announce that the results of the recent independent International Science Review of the larger UK National Measurement System (NMS) laboratories found our DI role to be "internationally leading" and "globally commended", delivering very high quality metrological services of high impact. This outcome reflects the passion, commitment and high scientific quality of the individuals delivering our NMS activities and clearly demonstrates the global position LGC holds in metrology.

With the announcement of the new UK government Industrial Strategy, we look forward to the opportunities that this will bring. The Strategy recognises the role measurement research, standards and skills development has to play towards growing the UK economy and we will continue to be actively involved in supporting its effective development to ensure social benefit. We have ambitious objectives to embed measurement reproducibility in pre-clinical research and support the development of measurement skills from apprenticeship to higher education and beyond through our involvement with Trailblazers, university Masters Programmes and a new centre for bio-analytical measurement science training.

Looking back, 2016 has seen a number of successes as we progress further towards growing and enhancing our position. Through our digital PCR (dPCR) facility we coordinated the most extensive comparison of dPCR performed to date, enabling the transfer of high accuracy materials, methods and approaches to data processing to a wide variety of global clinical stakeholders to support clinical method development. A unique rapid transportable assay for detecting the stress biomarker cortisol was developed this year and is being used for sports testing and healthcare applications. Our efforts to support the measurement needs of the biopharmaceutical industry are flourishing and, through a study involving multiple key industrial and academic collaborators, we will help provide increased confidence in the data provided to regulators for structural measurements of bio-therapeutics.Through our skills development facility we collaborated with UKAS to design and deliver a workshop to help clinical testing laboratories meet the quality requirements of the new ISO accreditation.

We are a partner in Innovate UK's new £6.5m funding programme Analysis for Innovators (A4I) which commences in early 2017 and will allow UK industry, particularly micro companies and SMEs, direct access to the unique measurement facilities that reside within LGC (as part of the NMS), NPL and STFC to facilitate growth and productivity. We look forward to the developments within this programme in the coming year.

This year LGC signed a further collaboration agreement with NIM, China's National Institute of Metrology and technical centre for legal metrology. This agreement, following on from the successful first collaboration signed in 2011, marks the next steps in the ongoing collaborative programme to develop new measurement capabilities and scientist exchanges in life science applications and reference material distribution.

We value our ongoing relationships with our partner and collaborator organisations, be they industry, clinical, academic or otherwise and will work ever closer with these to ensure translation of our measurement capability for maximum economic and social benefit.

I would like to thank all those responsible for delivering our work over this year for their commitment to maintaining the quality and consistency of chemical and bio-measurements.

Derek Craston
**Chief Scientific Officer**

**2016 achievements in numbers**

→ 29 peer-review publications
→ 10 new CMC claims
→ 12 reference materials
→ contributed to 22 ISO standards
→ 14 CCQM studies, leading 3
→ 267 delegates across 9 countries trained

# CONFIDENCE IN MEASUREMENT

For governments, society and individuals to have confidence in the decisions that are based on the thousands of routine measurements made each day they must also have confidence in the measurements themselves.

These measurements cover a vast array of applications, from clinicians using making a medical diagnosis, to labs providing forensic evidence to support the justice system, or tests to safeguard the quality of our water.

## REFERENCE MATERIALS

Reference materials (RMs) are the cornerstone of accurate and traceable measurements – they are measurement standards which can be used to validate analytical methods, establish traceability and support quality control.

LGC has a portfolio of over 150 materials covering high purity standards, carbon isotope ratios, food, environmental and clinical materials and alcohol standards.

LGC has accreditation to ISO Guide 34 as a Reference Material Produced and is a founder member of the European Reference Material co-operation established in 2004.


**New materials released in 2016:**

- ERM-AC022a Tacrolimus
- LGC7226 Goat

**Replacement materials released in 2016:**

- ERM-BD016a Sugar confectionary
- LGC7220 Horse meat
- LGC7221 Beef meat
- LGC7222 Pork meat
- LGC7240 1 % horse meat in beef
- LGC7242 1 % pork meet in beef
- LGC7241 10 % horse meet in beef
- LGC7243 10 % pork meet in beef
- ERM-AC404 5 % alcohol solution
- ERM-BD017a Sponge cake

# LGC'S LEADING ROLE WITHIN THE METROLOGY COMMUNITY (CCQM)

LGC regularly coordinates and participates in international CCQM comparison studies between metrology institutes, and holds a highly respected position within the metrology community. Successful participation in these studies supports our Calibration and Measurement Capabilities (CMCs) claims.

In 2016 we successfully participated in 14 studies (leading on 3) spanning the full range of our capabilities. Among these was the LGC-led study on isotope ratios in honey which involved National Measurement Institutes as well as expert laboratories contacted via the FIRMS (Forensic Isotope Ratio Mass Spectrometry Network). This study will support comparability of results for robust and reliable detection of food fraud across the supply chain, helping to ensure the safety and authenticity of our food.


Showing LGC's pivotal role in providing global equivalence of measurement and ensuring confidence of measurement within the UK

## SUPPORTING THE **"NEW SI"**

LGC scientists are participating in a CCQM study (P160) on isotope ratios and molar mass of highly enriched silicon which will help enable the new definition of the mole.

To ensure that the International System of Units continues to meet the needs of science, technology and commerce in the 21st century, the SI is being revised to be more accurate and remove reliance on the last physical artefact (kilogram). Under the “New SI” all units will be defined in terms of reference constants. The mole – the unit used within chemistry to describe how much of an atom or molecule is present – is being re-determined such that it is no longer dependent on the definition of the kilogram. Instead, a mole will be based on an actual measurement of the number of atoms (Avogadro’s constant).

This has been done by counting the number of atoms in a carefully machined 1 kg sphere of highly pure silicon-28, using the precise geometrical information of silicon crystallisation. However, to improve the accuracy of this number it is important to correct for the presence of trace amounts of other silicon isotopes in the manufactured single isotope crystal. To do so, the isotope ratios must be determined with very low uncertainty (20 parts per billion).

This CCQM study will help assess the level of measurement uncertainty achieved by participating measurement institutes for silicon isotope ratio measurements and ensure the new definition of the mole is appropriate for the future.

**Excellent performance at CCQM has maintained LGC’s world-leading position and also led to 10 new and revised CMC claims, including the first biological CMC claim for nucleic acid copy number using digital PCR.**

- Bio 006 DNA fragment copy number
- Inorg 026-028 uranium isotope ratios in renal fluids
- Inorg 040 arsenic in plant material
- Inorg 049 chromium species (VI) in water
- Inorg 050 electrolytes and elements in blood serum [revised]
- Inorg 051 electrolytes and elements in tissue [revised]
- Inorg 052 selenomethionine in blood serum
- Org 049 sirolimus purity

LGC scientists have been instrumental in the process of converting ISO Guide 34 to a conformity assessment standard in the 17000 series: ISO 17034 – General requirements for the competence of reference material producers. This new standard published in 2016 represents a global consensus for reference material production and has taken two years and significant international effort to achieve. LGC contributions included leading and coordinating the views of UK reference material stakeholders to inform the international position and providing comments throughout the drafting and production stages.

"LGC's coordination role helped to make sure that our UK representatives were well briefed on the technical problems facing the different reference material producers in the UK. LGC's reference material and international metrology experts were able to contribute strongly to the detailed technical provision of the new Standard. This new Standard provides a very good balance between essential requirement and those that need to be more flexible to allow for the very different kinds of reference materials needed in today's measurements"

Dr Steve Ellison, LGC Science Fellow and a UK Representative on the joint ISO CASCO/ISO REMCO Working Group

# STANDARDISING THE FUTURE OF MEDICINE

Cell therapies, where living cells are transplanted into a patient, have significant potential to treat and change the course of diseases currently unaffected by existing medicines.

Mesenchymal stem cells (MSCs) can differentiate (turn in to) fat, cartilage or bone cells. Although they can be isolated from a number of tissues, MSCs from bone marrow are widely used, with over 300 clinical trials run per year. These studies address a variety of conditions, including spinal cord injury, bone and cartilage repair, autoimmune diseases and cardiovascular disease, but with very mixed success. One significant reason for this is the variability in the quality of the cells after they are grown up in vitro to the numbers required for dosing (approx. 100-200 million cells per dose).

Scientists at LGC have been investigating the process of MSC expansion to identify appropriate selection criteria for MSCs of the required quality to be use in clinical trials. We have identified putative novel markers and measurements that could more quickly check and assess the ability of MSCs to differentiate or grow further without loss of potency than is currently available, reducing the time from weeks to days.

With hundreds of millions of pounds being invested in translating cell therapies from a research environment into effective clinical applications, there is a need for standardised quality controls to ensure appropriate selection of MSCs. This will ensure reproducibility of results and prevent funding being unnecessarily wasted in failed clinical trials.

Due to the complex and non-uniform nature of cell populations, developing standardised approaches for the bioprocessing of cells is crucial. LGC represents the UK on the ISO Technical Committee (TC 276 Biotechnology) that is developing best practice guides and standards for this field. We are leading on developing a best practice guide for users of ancillary bioprocessing materials (ISO 20399-3) and contributing to standards on guidance for cell counting methods (ISO 20391-1) and their statistical analysis (ISO 20391-2).

These guides and standards will improve the quality control and hence safety of cell-based products, supporting a more rapid progression of cell based therapies to the market place and making the future of medicine a reality for patients.

In collaboration with colleagues from Loughborough University we have established a UK Advisory Committee to represent the UK research and industry base and inform the ISO Biotechnology initiatives relating to manufacturability of cell-based therapies.

LGC and Desktop Genetics have been awarded funding from SynbiCITE, the UK's national centre for the commercialization of synthetic biology, to develop screening and validation tools for functional genomics, cell line engineering and synthetic biology. This will address the dire need in biology for a standardised approach to genome editing.

Our engagement with Loughborough University has led to the co-supervision of a PhD student with GSK to quantify the effect of operator variation attributed to flow cytometry analysis. This is part of a developing study to analyse variation when measuring different cell types.

## AT THE CENTRE OF ISOTOPE RATIO STANDARDISATION

Stable isotope ratio analysis provides valuable information across a wide variety of fields, including environmental studies, food analysis, forensics and geochemistry.

The scale used to certify existing reference materials for carbon isotope ratio measurements (VPDB scale) is defined through a series of artefacts, rather than a measurement process. Each time the reference standard needs replacing, the new material requires recalibration to the original sample, and the uncertainty increases.

These issues are being addressed by the IAEA (International Atomic Energy Agency), one of the central bodies responsible for the standardisation of light element isotope ratios. In 2016, LGC was invited to an IAEA Technical Meeting on Stable Isotope Reference Products to present the work involved in developing our reference materials certified for absolute carbon isotope ratios. We were subsequently asked to join three new IAEA Working Groups covering the production of isotope ratio reference material production, effective communication and terminology standardisation.

This invitation recognises the expertise and reputation LGC has in the area of isotope ratio analysis and will ensure LGC inputs at the highest level to inform and support good measurement practice.

Through our engagement with supporting bodies in the isotope ratio community such as the IAEA (International Atomic Energy Agency), the need for multiple carbon isotope ratio reference materials that form a calibration series was identified. In response to this, LGC is currently producing three reference materials in solution at differing 13/12-C isotope ratios. These materials, produced under LGC's ISO Guide 34 accreditation, will be released in 2017.

# HOW CERTAIN CAN YOU BE: THE NEED FOR MEASUREMENT UNCERTAINTY

To have a real understanding of the value of a measurement you need to know both the quantity and its quality, i.e. how good is the measurement and can you trust it?

Measurement uncertainty allows individual measurement results to be meaningfully compared, for example to see whether a clinical limit has been exceeded or whether results produced before and after a drug intervention are significantly different. In some cases, such as a quick screening test, a large measurement uncertainty may be acceptable but in others, for example monitoring the amount of a chemotherapy drug present in the body, a small measurement uncertainty is necessary. The impact on human health, the environment and the economy can be significant if measurement uncertainty is not sufficiently accounted for.

Recently the UK adopted the ISO 15189 standard (Medical laboratories – Requirements for quality and competence) as a requirement for the accreditation of clinical laboratories. The standard requires measurement uncertainty to be calculated for each clinical assay.

LGC has been a leading exponent of calculating measurement uncertainty, and its use in the interpretation of measurement results for many years. Using this expertise we collaborated with UKAS to design and deliver a well-received workshop to help clinical testing laboratories meet the quality requirements of this new accreditation.

The first workshop trained 20 delegates from 15 clinical laboratories. With a long waiting list demonstrating the demand for further training in this area, the course will be run again in 2017.

"Very valuable course – helped with overall understanding and also had useful discussions with other clinical scientists"

# THERAPEUTIC DRUGS

In the clinic, certified reference materials are required to help remove measurement variation between hospitals, ensure more precise prognoses and ultimately improve patient care.

Immunosuppressants, the therapeutic drugs used to prevent patients rejecting a donor organ, have a very narrow therapeutic range. Improving the accuracy of immunosuppressant monitoring through the use of higher order reference standards could reduce the number of rejections and give patients the best possible chance of an improved quality of life. Successful aftercare of donor organ patients is estimated to save the NHS at least £150 million each year through, for example, savings of dialysis costs, as well as give the 4,500 patients annually who undergo transplants the best possible chance of an improved quality of life.

Over the past few years LGC has been producing reference methods and certified reference materials for two commonly prescribed immunosuppressants – tacrolimus and sirolimus – to underpin the standardisation of existing or in-development assays.

New materials have been released this year to extend the current portfolio and support a greater number of laboratories, secondary standards producers and assay developers ensure compliance with ISO 15189, ultimately helping ensure consistent care across transplant centres globally.

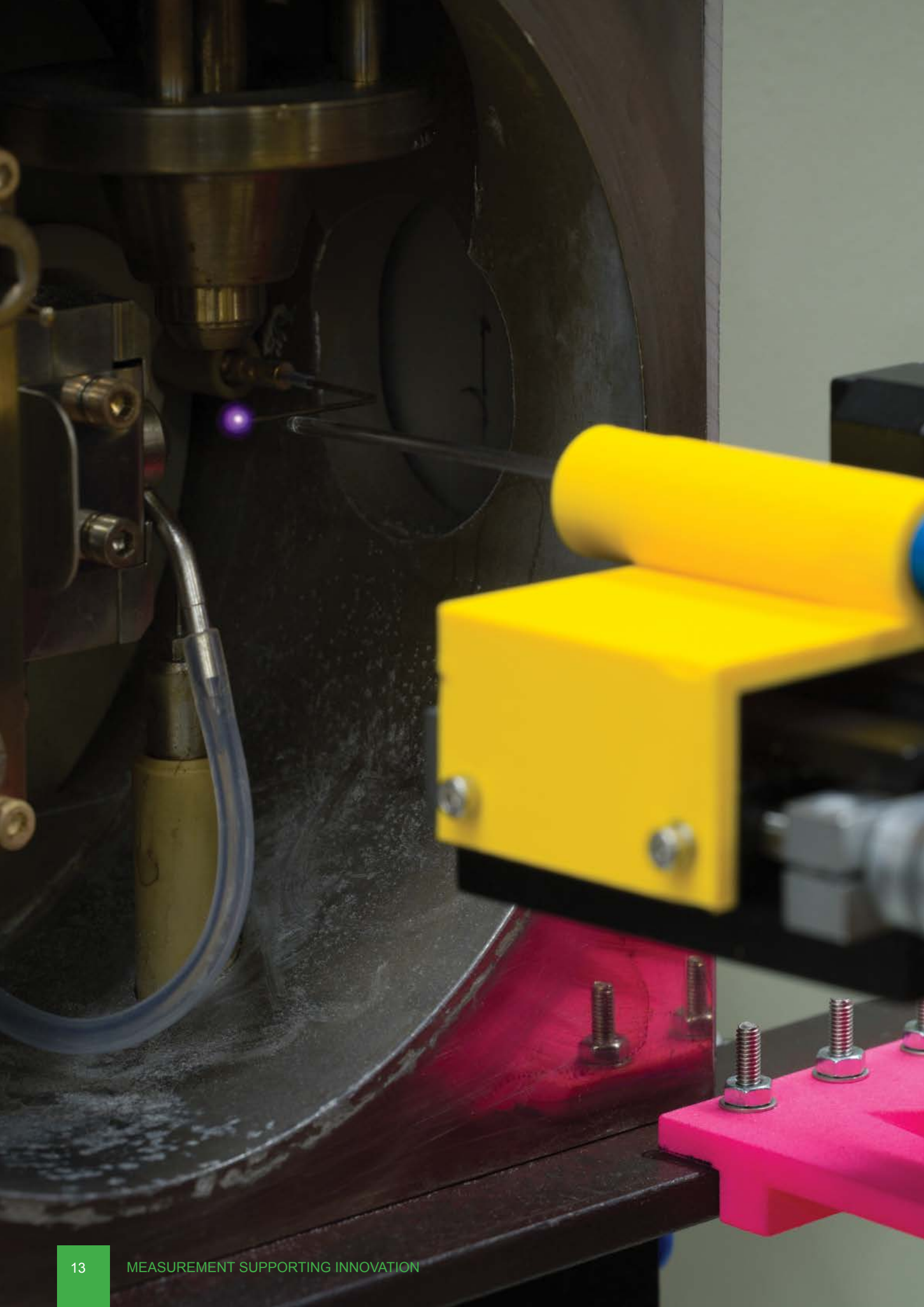
LGC scientists were invited to attend an international symposium hosted by BIPM and WADA on standards and the importance of measurement accuracy in anti-doping analysis. They outlined approaches to measurement uncertainty and qualitative analysis and their input will help experts in anti-doping analysis to support the harmonization of analytical practices and ensure clean competitive sport.

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

The reference method developed for tacrolimus in whole human blood was used to support Waters to validate their Marked MassTrak™ Immunosuppressant assay, which is FDA 510(k) cleared and conforms to the European In Vitro Diagnostics Directive (98/79/EC).

"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."

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



# MEASUREMENT SUPPORTING INNOVATION

Through our DI role we support innovation within measurement science, providing novel measurement solutions to bridge the gap from fundamental research to application in industry.

By responding to new measurement challenges as they develop, we can support industry to make positive changes, improve processes and technologies more quickly and effectively and reduce the risks associated with development. This will help to increase productivity and improve quality of life across the UK.

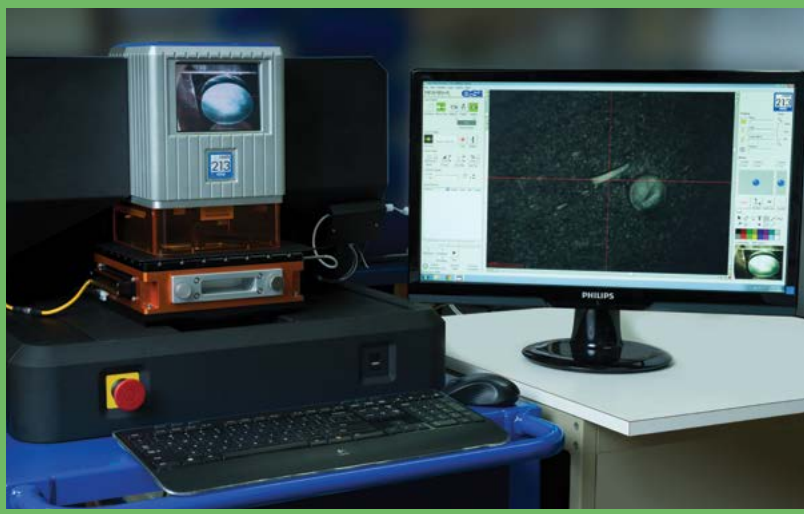
## NOVEL MERCURY MEASUREMENTS FOR AIR FILTERS

Mercury in its many chemical forms is highly toxic. The UNEP Minamata Convention (signed in 2013) is a global treaty designed to protect human health and the environment from the adverse effects of mercury, providing, for example, control measures on its release into the environment. In order to understand the ongoing effects of mercury on humans and the environment it is crucial to be able to accurately measure these levels to assess concentrations and trends.

At LGC we have been working with other European measurement institutes as a partner in an EU-funded project (known as 'MeTra') to help provide the measurement infrastructure to support current EU legislation, ensure the quality and comparability of mercury measurement results and underpin advanced analytical techniques of the future. As there are currently no EU-approved methods for mercury in air, we have developed a novel high accuracy, direct analysis method using inorganic mass spectrometry combined with laser ablation (LA-ICP-MS). This has been applied to real-world environmental samples (air filters) from rural and urban environments.

These results will feed into the UK and EU committees on air quality (BSI EH/2/3, CEN TC264) and will help to provide the evidence base for the next generation of standard methods for air quality assessment.

Following on from the success of this project, LGC won additional funding in 2016 for a subsequent project under the European Metrology Programme for Innovation and Research (EMPIR). This project ("Metrology for oxidised mercury") is funded under the challenge 'metrology for environment' and will support the effective environment control of mercury and its different forms in gas emission sources and in the atmosphere.



# TOWARDS IMPROVED CONTROL IN BIO-MANUFACTURING

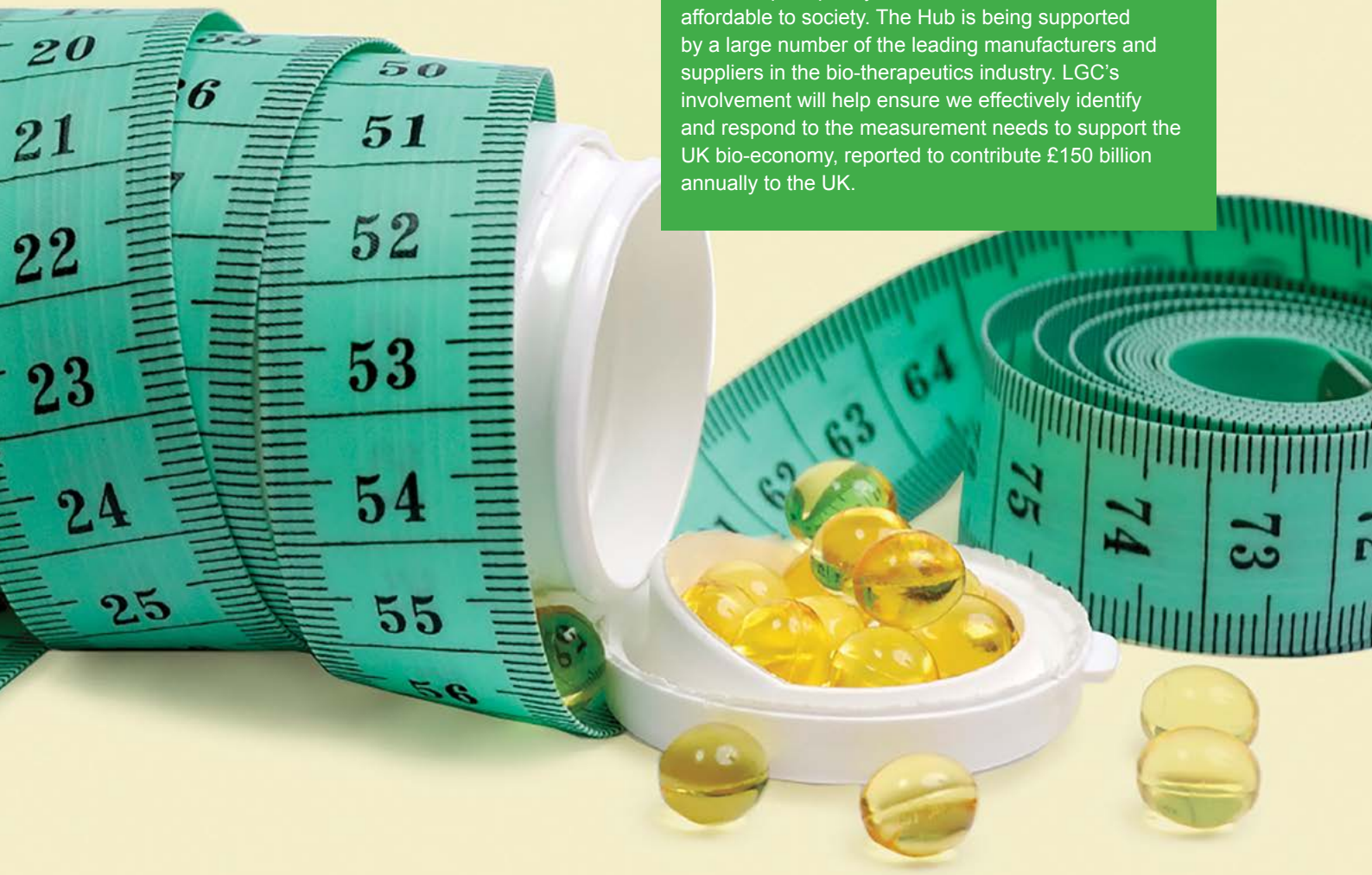
Biopharmaceuticals represent the largest growing area of the pharmaceutical sector. The higher order structure (secondary and tertiary structure) of these bio-products are critical quality attributes for determining their stability, efficacy and safety. If changes in the manufacturing process occur or a proposed product has to be proven to be (bio)similar to an original, the same critical quality attributes must be demonstrated. Consequently there is a need for higher order protein structure measurements to be performed throughout product development and manufacturing (ICH Q6B, ICH Q5E).

Several physical and analytical methods are available for higher order protein structural analysis. However, how to select the most appropriate method, compare data across methods or benchmark new techniques are all still areas of major concern to the biopharmaceutical industry.

To help address these challenges, LGC is co-ordinating an inter-laboratory study using a well-characterised and easily accessible protein model system (WHO recombinant human growth hormone in the presence of increasing concentrations of Zn). This study, involving multiple industrial and academic collaborators, will evaluate the sensitivity of different methods to structural changes.

We envisage the results of this study will help improve control in bio-manufacturing, increase confidence in the data provided to regulators and generate data for quality control and to benchmark novel analytical techniques.

LGC is a partner in UCL's new EPSRC Future Targeted Healthcare Manufacturing Hub. The Hub will address manufacturing, business and regulatory challenges to ensure that new targeted biological medicines can be developed quickly and manufactured at a cost affordable to society. The Hub is being supported by a large number of the leading manufacturers and suppliers in the bio-therapeutics industry. LGC's involvement will help ensure we effectively identify and respond to the measurement needs to support the UK bio-economy, reported to contribute £150 billion annually to the UK.

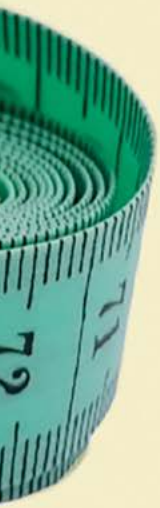


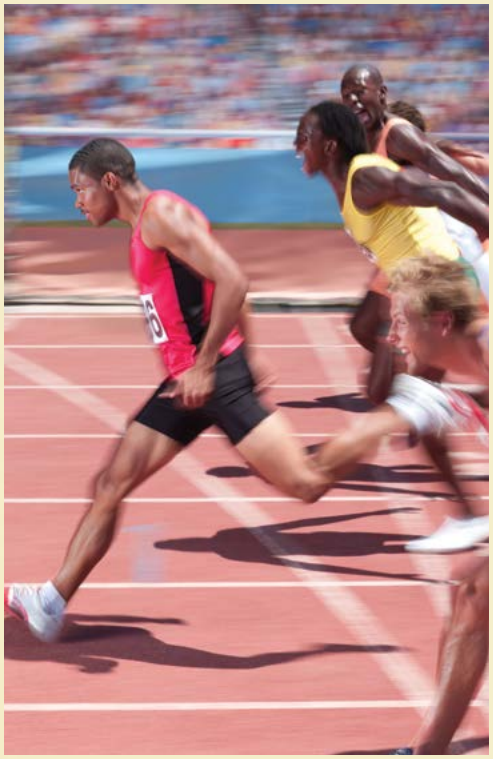
## THE STRESS OF COMPETITION: A NOVEL APPROACH

"As the world of sports science changes rapidly, so does expectation from coaches and athletes in understanding the training process in greater detail, more reliably and rapidly. Traditionally, most hormonal samples are collected either through venepuncture (blood) or saliva. Samples are then taken back to a laboratory, frozen and analysed a few weeks later. This can represent a cumbersome and inefficient process if we are to provide coaches and athletes with up-to-date information that informs the training process in the 'here and now' rather than the past."

Brian Cunniffe, Performance Lead at the English Institute of Sport

Stress and anxiety are important clinical indicators for patients suffering from Alzheimer's or Parkinson's diagnosis. This assay is being used in a new patient-centric EU-funded project ('NeuroMET') involving national measurement institutes, clinicians and academics. This is the first metrology study to recruit patient cohorts and aims to correlate patient centre outcome measures against clinical biomarkers to improve diagnosis, and more effectively predict patient decline and treatment procedures.





Stress biomarkers, such as cortisol, are often used to monitor the effectiveness of an athlete's training regime. However, levels of cortisol change quickly following exercise and so need to be monitored trackside to determine whether an athlete needs to be rested or whether they can train further and harder the next day.

Researchers at LGC have developed a unique new assay for detecting both free and total cortisol within human serum using a transportable platform technology. In collaboration with the English Institute of Sport, the assays were evaluated using blood samples from athletes (pre- and post-training) at Loughborough University via a pin prick to the finger.

Our approach successfully eliminates the need for sample processing and reduces the analyte incubation to minutes, negating the need to transit samples to laboratories and providing athletes with further information.

This may in the future provide more robust results for athletes on which to base their training decisions and help increase the return on investment on the hundreds of millions of pounds spent on UK elite athletes.

# DIGITAL PCR: COUNTING AND CANCER

Accurate counting of biological entities underpins many sectors including healthcare, security, environment, biotechnology and food. This can range from monitoring viral load or circulating tumour cells in patients to identifying the presence of GMOs in foods. However, a lack of higher order reference methods and materials has been a major hindrance in supporting measurement comparability, promoting translation of these approaches to the clinic and ensuring regulatory compliance.

LGC coordinated an EU-funded consortium of national measurement institutes, academics and industrial partners (known as 'Bio-SITrace') to address this challenge. The project focused on developing a measurement framework to enable traceability of bio-molecules to the SI, assessing approaches to characterise pure nucleic acid calibration standards and developing new reference methods for nucleic acid, protein and cell measurements based on single-molecule detection and counting ('enumeration').

The applicability of digital PCR (dPCR) as a reference method has been demonstrated at LGC through enumeration of a DNA mutation in a cancer gene (KRAS) and validated through an inter-laboratory study involving 7 national measurement institutes. This reference method can now be used by reference material producers and may form the basis of calibration services provided to nucleic acid-based IVD manufacturers. The resultant guidelines for method validation and uncertainty calculation will enable the development of reference methods for cancer and other clinically relevant targets in the future.

LGC coordinated the most extensive comparison of dPCR performed to date: an inter-laboratory study involving 21 independent end-user laboratories to quantify a low-level cancer mutation. This highly successful study, performed in collaboration with the instrument manufacturer Bio-Rad, confirmed that dPCR can perform highly reproducible absolute quantification at very low levels (<1 %) and enabled the transfer of high accuracy materials, methods and approaches to data processing to a wide variety of global clinical stakeholders.

The results of this study will help support the development of clinical methods for the detection of rare sequence variants, for example in cancer or prenatal diagnostics, monitoring of transplant organ rejection or infectious diseases.

Biomolecular entities cannot be described in terms of the seven base quantities of the International System of Units (SI) but can still be counted. Guidance is required to ensure this is done to establish traceability for this kind of measurement.

Recommendations and text for inclusion in the latest revision of the SI brochure were proposed as a result of BioSITrace to describe how cellular or biomolecular entities can achieve formal traceability:

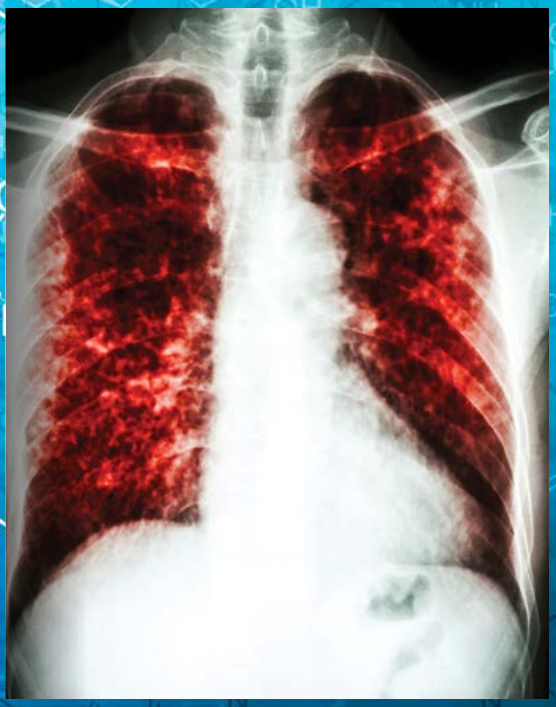
A modified reference exemplifying counting of "a number of cellular or biomolecular entities (e.g. copies of a particular nucleic acid sequence)" and "formal traceability to the SI can be established through appropriate, validated measurement procedures."

These modifications were approved by the Consultative Committee for Units and endorsed by the CCQM Nucleic Acid Working Group in 2016 with final ratification by the General Conference on Weights and Measures (CPGM) expected in 2018.

LGC won additional funding in 2016 from the European Metrology Programme for Innovation and Research (EMPIR) to help address the challenge of 'support for metrology impact'. This project ("New underpinning standards for improved bio-analytical measurement in Biotechnology & In vitro Diagnostics") will support contributions to biological ISO standards. It utilises the best practice guidance generated in previous LGC-led European-funded metrology projects (Bio-SITrace, INFECT-MET).

The enumeration study and standardisation initiative were highlighted and positively endorsed at an international congress (4th Joint EFLM-UEMS Congress, Warsaw) by the Chair, Prof Dr Michael Oellerich, the European Director of the World Association of Societies of Pathology and Laboratory Medicine (WASPaLM). LGC has been invited to develop a workshop on the issue for clinicians and pathologists at the 2017 WASPaLM congress.

Using digital PCR and in collaboration with the Royal Free Hospital, a reference method was developed at LGC for the accurate quantification of the bacterium that causes tuberculosis (TB). A global inter-laboratory comparison study for tuberculosis quantification run by LGC highlighted the potential limitations of bacterial biomarker identification when a metrological approach is not taken. As a result of this study the multinational TB clinical trials consortium PanACEA will change their choice of biomarker.



# PEOPLE

**Dr Jim Huggett** was part of the group awarded the European & Developing Countries Clinical Trials Partnership (EDCTP) Outstanding Research Team Award at the 2016 EDCTP Forum in Zambia. The award, presented by the President of the Republic of Zambia, was received for the University of Zambia and University College London Medical School (UNZA-UCLMS) partnership for their work against killer infectious diseases, particularly TB and HIV/AIDS.

**Dr Sarah Hill** won a prize at the Biennial National Atomic Spectroscopy Symposium for her poster describing reference value assignments of iodine.

**Dima AlMekdad**, part-time student at LGC and King's College London, was awarded a place at the prestigious SET for BRITAIN event at the House of Commons for early-career research scientists.

**Dr Tamara Lekishvili** won a prize at the 5th Flow Cytommetry UK meeting for her poster describing a novel method for quality assessment of human mesenchymal stromal cells.

**Kate Groves** received a poster prize at the JCTLM Workshop on Protein and Peptide Therapeutics Diagnostic Research and Quality Assurance for her work on protein structural analysis.

**John Entwisle** received a poster prize for "significant innovative analytical research", sponsored by Analytical Bioanalytical Chemistry, at the Nordic Conference on Plasma Spectrochemistry for his work on chromium speciation in water.

**John Warren** has been elected to represent EURAMET (the European Regional Metrology Organisation) on the CCQM Key Comparison Working Group (KCWG), the group responsible for overseeing the review of CMCs, defining technical review criteria and co-ordinating the inter-regional review process. This appointment recognises LGC's standing amongst European NMIs.

**Dr Jim Huggett** was appointed to a Senior Lectureship position in Analytical Microbiology within the School of Biosciences and Medicine at the University of Surrey. This position denotes the start of a sustained and deeper partnership for LGC with the University.

**Dr Dorota Bartczak** was invited to be the UK Representative on the European and ISO Committees TC for Nanotechnologies (CEN TC 352, ISO TC 229) on behalf of the British Standards Institution, recognising LGC's expertise and reputation in the area of nanotechnology measurement.

**Dr Adam Cryar** was invited on to the Steering Committee of the London Biological Mass Spectrometry Discussion Group, a group sponsored by the British Mass Spectrometry Society and the RSC Separation Science Group.

**Dr Heidi Goenaga-Infante** was invited to become a Fellow of the Royal Society of Chemistry (FRSC). She and her team are at the forefront of research into the determination of product authenticity, food safety and fraud detection using a range of mass spectrometry methods and their leading-edge research into nanoparticles is having an impact in the clinical and environmental sectors.

# KNOWLEDGE TRANSFER & DISSEMINATION

## TRAINING FOR THE FUTURE

LGC has 19 years' experience in delivering analytical quality training programmes to customers worldwide. The courses focus on providing analysts with the tools to ensure the validity of their measurement results.

LGC scientists produced a new freely available best practice guide to support those working in a molecular biology laboratory: **Practical laboratory skills for molecular biologists.** The guide covers the skills required to produce valid results and requirements relating to the nature of the materials being handled in a molecular biology laboratory and has already been downloaded over 500 times.

Developing the measurement knowledge and skills of the next generation of scientists is essential to ensuring the future growth and competitiveness of UK industries. LGC is collaborating with leading universities to develop and deliver masters-level courses to ensure the fundamentals of measurement science are addressed.

**We delivered 19 courses in 9 countries**
**We trained 267 delegates from 65 organisations**

We have an extensive programme of courses that is delivered from our headquarters in Teddington. Courses can also be delivered at customer sites and customised, if required, to meet specific training requirements.

**Topics covered include:**

Method validation – Learn how to demonstrate that test method are fit for purpose

Evaluating measurement uncertainty – The principles and practice of estimating measurement uncertainty in testing laboratories

Statistics for analysts – Getting the most from data generated in the laboratory

Designing effective experiments – Learn how to plan, execute and analyse efficient experiments

Understanding ISO/IEC 17025 requirements for analytical laboratories – Improving awareness of the technical requirements of ISO/IEC 17025

Using proficiency testing in the analytical laboratory – Learn how to get the maximum benefit from participation in proficiency testing schemes

Reference material production – Planning effective reference material characterisation studies to meet the requirements of ISO Guide 34.

Our courses consistently receive excellent feedback from delegates and we have a high level of repeat customers. Over 97% of delegates who completed a course feedback questionnaire in 2015 stated that the training met their expectations.

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# SELECTED PUBLICATIONS

The quality and credibility of our science is demonstrated in part through our publications in peer-reviewed journals. In 2016 LGC experts published 29 scientific papers. Here is a selection:


Alikian M et al. RT-qPCR and RT-Digital PCR: a comparison of different platforms for the evaluation of residual disease in chronic myeloid leukaemia. Clin Chem (2016) 63(2)525-31. DOI: 10.1016/j.clml.2016.07.081

Archibald PRT et al. Comparability of scalable, automated hMSC culture using manual and automated process steps. Biochem Eng J (2016) 108:69-83. DOI:10.1016/j.bej.2015.07.001

Deitrich C et al. Accurate quantification of Selenoprotein P (SEPP1) in plasma using isotopically enriched seleno-peptides and species-specific isotope dilution with HPLC coupled to ICP-MS/MS. Anal Chem (2016) 88(12)6357-65. DOI: 10.1021/acs.analchem.6b00715

Estela del Castillo Busto M et al. Accurate quantification of selenoproteins in human plasma/serum by isotope dilution ICP-MS: focus on selenoprotein P. J Anal At Spectrom (2016) 31:1904-12. DOI: 10.1039/C6JA00122J

Fardus-Reid F, Warren J, Le Gresley A. Validating heteronuclear 2D quantitative NMR. Anal Meth (2016) 8:2013-19, DOI: 10.1039/C6AY00111D
*top-25 most downloaded article for 2016*

Gollwitzer C et al. A comparison of techniques for size measurement of nanoparticles in cell culture medium. Anal Methods (2016) 8:5272-82. DOI: 10.1039/C6AY00419A

Malinovsky M, Dunn PJH, Goenaga-Infante H. Calibration of Mo isotope amount ratio measurements by MC-ICPMS using normalisation to an internal standard and improved experimental design. J Anal At Spectrom (2016) 31:1978-88. DOI: 10.1039/C6JA00184J

Phelan J et al. The variability and reproducibility of whole genome sequencing technology for detecting resistance to anti-tuberculous drugs. Genome Med (2016) 8:132-40. DOI:10.1186/s13073-016-0385-x

Swart C et al. Potential reference measurement procedures for PBDE in surface water at levels required by the EU Water Frame Directive. Talanta (2016) 152:251-258. DOI:10.1016/j.talanta.2016.01.066

Whale AS et al. An international inter-laboratory digital PCR study demonstrates high reproducibility for the measurement of a rare sequence variant. Anal Chem (2016). DOI: 10.1021/acs.analchem.6b03980 E-pub ahead of print

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Wilson PJ & Ellison SLR. Extending digital PCR analysis by modelling quantification cycle data. BMC Bioinformatics (2016) 17:421. DOI: 10.1186/s12859-016-1275-3 open access

Williams DJ et al. Comparability: manufacturing, characterization and controls, report of a UK Regenerative Medicine Platform Pluripotent Stem Cell Platform Workshop. Regen Med (2016) 11(5)483-92. DOI:10.2217/rme-2016-0053

Yoo H-B et al. An international comparison of enumeration-based quantification of DNA copy-concentration using flow cytometric counting and digital polymerase chain reaction. Anal Chem (2016) 88(24)12169-76. DOI:10.1021/acs.analchem.6b03076


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