NML
UK NATIONAL MEASUREMENT LABORATORY
FOR CHEMICAL AND BIO-MEASUREMENT
HOSTED AT LGC

ANNUAL REVIEW | **2018**

Department for Business, Energy & Industrial Strategy
FUNDED BY BEIS

LGC

Thousands of decisions that affect our everyday lives are based on measurements.

To be able to rely on these decisions, there must be confidence in the measurements themselves.

EXECUTIVE SUMMARY

2018 was a special year for us, as it marked the thirtieth anniversary of the establishment of the UK's National Measurement Laboratory for chemical and bio-measurement, hosted at LGC.

In 1988, Government Chemist Alex Williams, seeing the need for improved quality of analytical measurements, initiated and launched the Valid Analytical Measurement (VAM) programme to develop a chemical measurement infrastructure in the UK. The UK was one of the pioneers within the global measurement community to recognise the need to address the new and developing challenges of measurement across chemistry and biology. This programme would go on to evolve into the NML at LGC as we know it today.

In our thirty years of performing measurements to support the UK, we've experienced significant growth, seen big changes in the challenges we've been set and made some major breakthroughs. Today, we address a complex set of cross-sector issues, providing advice, setting standards, developing reference methods, informing legislation and resolving disputes.

Our work covers fundamental and emerging measurement research in advanced therapeutics, clinical diagnostics, safety and security and underpins some of the biggest challenges of our time, including neurodegenerative diseases, food safety, cancer and anti-microbial resistance. In addition to our government funded research programmes, we provide measurement services to our customers, through contract R&D, specialised calibration services, provision of high order reference materials, analytical quality training and consultancy.

"In my role, I am fortunate to be able to see the major benefits that chemical and biological measurements make to the prosperity of companies and the lives of individuals across areas as broad as clinical diagnosis, drug development, environmental protection and food security. Indeed, in a global economy, with complex supply chains and regulatory frameworks, it is hard to see how many markets could function without it.

Derek Craston
Chief Scientific Officer

OUR NATIONAL ROLES

We are the UK's designated institute for chemical and bio-measurement and support the work of the Government Chemist.

We are sponsored by BEIS as part of the National Measurement System group.

We ensure trust and confidence in chemical and bio-measurements in the UK to support government and industry needs.

We address measurement challenges of the future to foster innovation, promoting productivity and economic growth.

OUR LOCATIONS

Our Cell Metrology Laboratory has been relocated to Fordham, Cambridgeshire.
This will allow closer integration with the cutting-edge research being performed in and around the Cambridge area and enable our Cells team to more effectively address the emerging measurement challenges surrounding the development of advanced healthcare solutions.

- Centres of excellence
- Academic collaborations/joint PhDs

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www.lgcgroup.com/nml

WE WORK IN **PARTNERSHIP** WITH INDUSTRY, NHS, GOVERNMENT AND ACADEMIA

OUR LEVERAGED INCOME **FROM ALL SERVICES WAS** **£2.8 MILLION**

OUR NUMBERS 2018

30 PEER-REVIEW PUBLICATIONS

2 NEW ISO ACCREDITATIONS

15 REFERENCE MATERIALS

20 (7 PUBLISHED) CONTRIBUTIONS TO ISO STANDARDS

WE WORK WITH **OVER 590 DIFFERENT ORGANISATIONS**

THE NML AND THE GLOBAL THE MEASUREMENT COMMUNITY

WE WORK **GLOBALLY** TO **STANDARDISE** MEASUREMENT SCIENCE

As part of our role representing the UK to ensure international standardisation, we regularly coordinate and participate in inter-comparison studies with other countries' National Measurement Institutes, under the auspices of the Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM). We are regarded as one of the top institutes for our designation within the global measurement community. Successful participation in these studies supports our Calibration and Measurement Capabilities (CMCs) claims which underpin our measurement services.

6 (3 LEADING) **CCQM** STUDIES

Excellent performance at CCQM this year has led to 2 new CMC claims. We became the first measurement institute to be granted a broad scope CMC claim for solid peptide purity analysis. This, combined with our new broad scope claim for high purity calibration solutions, will further underpin our purity capabilities to produce and value-assign high purity reference standards to meet the growing requirement for a greater diversity of pure materials.

2 **NEW CMC** CLAIMS

EUROPEAN FUNDING SUCCESS

This year we won an additional £1.6m of funding under the European Metrology Programme for Innovation and Research (EMPIR) to enhance our measurement research activities. EMPIR coordinates research projects to address the EU's Grand Challenges, while supporting and developing the SI system of measurement units.

Over the next three years, the new projects will address measurement challenges associated with novel biomarker discovery (extracellular vesicles) and improving accurate diagnostic methods (cardiac markers, sepsis management, neurodegenerative diseases), and develop standards and best practice guidelines for nanoparticle characterisation.

EUROPEAN METROLOGY NETWORKS

We are also partners in two of the newly established European Metrology Networks (EMNs) that will provide a sustainable structure for ongoing close collaboration in measurement science across Europe. Through the EMNs, new activities and services that address the needs of the respective stakeholder communities will be developed.

SUPPORTING TRACEABILITY IN LABORATORY MEDICINE

In vitro diagnostics (IVDs) are clinical tests that analyse samples taken from the patient to help clinicians detects diseases or diagnose a medical condition. Performing these tests accurately, regardless of the laboratory or instrument used for testing, is crucial for the wellbeing of patients. Traceability is a fundamental component in achieving this.

The TraceLabMed EMN aims to become the European gateway for coordinating activities and services concerning the traceability of laboratory measurement results based on in vitro diagnostics.

We are leading work with IVD manufacturers to understand the measurement challenges they face in conforming to new traceability and uncertainty requirements of recently implemented regulation (EU IVDR 2017/746). Supporting industry in meeting these regulatory requirements will allow them to safely maintain market access and help justify public confidence in laboratory test results.

SUPPORTING THE MATHEMATICS BEHIND THE MEASUREMENTS

Mathematical modelling and statistics are crucial for advanced measurements that address a wide range of challenges. From sustainable energy to environmental monitoring, healthcare to advanced manufacturing, these challenges increasingly depend on both new measurement approaches and new and increasingly complex data analytics, such as machine learning, multi-scale modelling and artificial intelligence.

The MathMet ("Mathematics for Metrology") network will provide a single reference point for the mathematical and statistical activities needed to tackle these new challenges, helping to develop the mathematical tools to support measurement in these areas of strategic importance.

Our expertise in statistics and uncertainty estimations will help support this network, as well as providing an important perspective of the needs of the users of chemical and biological measurements.

REFERENCE MATERIALS AND UNDERPINNING MEASUREMENTS

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.

We have a portfolio of over materials covering high purity standards, carbon isotope ratios, food, environmental and clinical materials, and alcohol standards. This year we released materials to protect food authenticity and safety, and support regulation around consumer products.

OUR QUALITY ACCREDITED TO
ISO17025
ISO17034
ISO9001

NEW MATERIALS

LGC171-KT	glycine solutions certified for absolute carbon isotope ratio

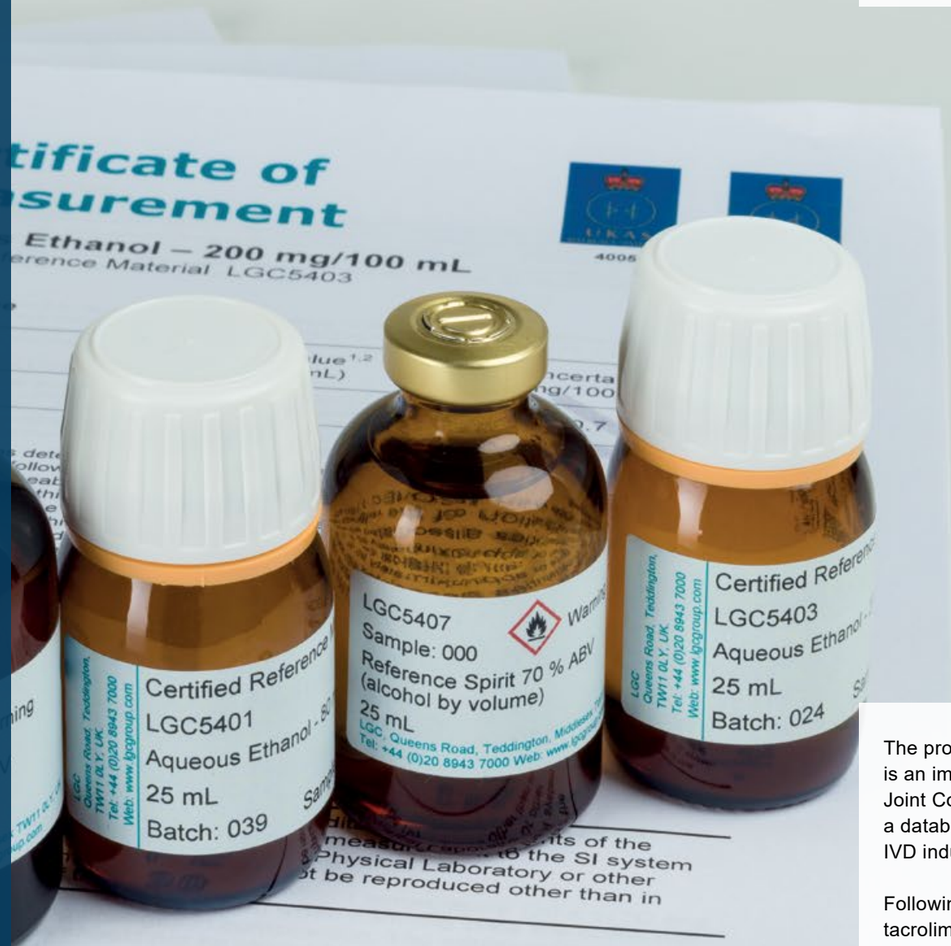
REPLACEMENT MATERIALS

LGC5403	aqueous ethanol CRM for forensic applications
LGC6027	soft drinking water for metals
LGC8211	frozen human serum - elements and selenomethionine

Meat authenticity materials

LGC7211	1% pork meat in beef
LGC7220	horse meat
LGC7221	beef meat
LGC7222	pork meat
LGC7223	sheep meat
LGC7224	chicken meat
LGC7225	turkey meat
LGC7420	1% horse meat in beef
LGC7426	1% turkey meat in sheep
LGC7428	1% beef meat in sheep
LGC7474	1% chicken meat in sheep

This year we successfully completed the transition from ISO Guide 34 to ISO 17034:2016 accreditation after assessment by the United Kingdom Accreditation Service (UKAS). This transition supports our role as a reference material producer making materials in accordance with internationally agreed best practice, providing an independent assessment of our capabilities.



We have been awarded ISO/IEC 17025 accreditation for the quantification of DNA using digital PCR by the United Kingdom Accreditation Service (UKAS). We are one of the few laboratories worldwide to have gained this accreditation.

Our DNA Measurement Laboratory provides independent and authoritative quantitative measurements of DNA. Such measurements are used to assist the development and validation of new assays and technologies, which support the characterisation of biological reference materials and regulatory compliance.

We have been appointed as an expert laboratory by the external quality assurance testing provider INSTAND e.V. The appointment, which covers external quality assurance in the field of virus genome detection, recognises our world-leading expertise in the field of digital PCR for nucleic acid quantification.

> The NML is recognised internationally as being at the leading-edge of applying dPCR techniques to standardise and therefore improve diagnostic laboratory measurements so that we can better diagnose and treat patients and improve virus safety testing in blood transfusion.

Heinz Zeichhardt, EQAS Adviser, Charité-Universitätsmedizin Berlin

The production and adoption of reference materials and reference methods is an important step to ensure accurate laboratory medicine test results. The Joint Committee for Traceability in Laboratory Medicine (JCTLM) maintains a database of these higher order materials and methods to help support the IVD industry to meet the traceability requirement of the EU IVD Directive.

Following a peer review process, our certified reference material for tacrolimus, an immunosuppressant drug, was accepted for listing on the JCTLM database (ERM-AC022a Pure Tacrolimus).

SUPPORTING THE NHS

Measurement plays a fundamental part in providing safe and effective patient care; underpinning quality, enabling innovation and supporting the development of new treatments and diagnostics. The NML is proud to be one of the partners in the NHS Chief Scientific Officer's Knowledge Transfer Partnership (KTP) programme, a joint initiative between NHS England and the laboratories and organisations that deliver the UK's National Measurement Strategy.

The 12 month programme provides healthcare scientists with the opportunity to work alongside leading measurement scientists, building long-term collaborations and exchanging skills and expertise to improve and enhance patient care within the NHS, in line with the NHS Long Term Plan.

In the second year of this programme, we have worked with clinical scientists from across the country to address measurement challenges including antimicrobial resistance monitoring, genomic testing and disease diagnostics.

"This [programme] is a fantastic opportunity for clinical leaders in their fields to harness new technology and innovation to transform services, improve outcomes and reduce cost through academic, clinical and industry partnership.

Professor Sue Hill OBE, Chief Scientific Officer for NHS England

NEW TESTING APPROACHES FOR LUNG CANCER TESTING

Lung cancer is the most common cause of cancer death in the United Kingdom (21%) with one specific type (non-small-cell lung cancer, NSCLC) accounting for more than 85% of all these cases. Genetic testing of DNA from tumour samples obtained from NSCLC patients can help personalise their treatment and improve their survival rates and quality of life and survival.

We are working with Dr Nicholas Hickson at the Manchester Genomics Diagnostics Laboratory, part of the Manchester University NHS Foundation Trust, to help validate a non-invasive test ('liquid biopsy') for NSCLC diagnosis. This approach, combining purifying tumour DNA from blood or urine with next generation sequencing, would be the first example of its kind to be used in an NHS genetic diagnostics laboratory.

This work will enable personalised selection of therapies based on the specific genetic mutations in the patient's lung cancer, allowing for targeted cancer and further improving patients outcomes.

IMPROVING COMPARABILITY AND DIAGNOSIS

High blood pressure (hypertension) affects more than 1 in 4 adults in the UK and is the third biggest risk factor for premature death. It is thought that up to 10 % of patients may have a specific underlying condition (primary hyperaldosteronism) causing their high blood pressure. This condition must be managed differently to other forms of hypertension.

Diagnosis requires accurate quantification of the steroid hormone aldosterone and its relation to the blood pressure enzyme renin. However, there is currently no easy to use reference method for quantifying aldosterone.

We are working with the Manchester University NHS Foundation Trust and the University of Manchester under the NHS Knowledge Transfer Partnership programme to develop a traceable mass spectrometry method for aldosterone.

This method will then be used to assign values to Proficiency Testing (PT) schemes used in routine laboratories to improve comparability of results, helping to prevent misdiagnosis of hyperaldosteronism and ultimately improving patient care.

NOVEL TECHNOLOGY FOR ANTIMICROBIAL RESISTANCE MONITORING

Antimicrobial resistance (AMR) is becoming an increasingly serious threat to global public health, putting at risk our ability to treat common infections and making a post-antibiotic era a very real possibility for the 21st century. New generations of DNA sequencing techniques could provide highly accurate detection of antibiotic resistance, including for organisms that are currently beyond the capability of current routine microbiological testing.

The development of smaller and faster technologies (e.g. nanopore sequencing) could move these tests out of laboratories to become point of care devices.

However, for their successful adoption into routine testing, standardisation is critical. We are working with Dr Kathryn Harris at Great Ormond Street Hospital to evaluate the performance of these novel sequencing devices, where they could improve the patient care and support the UK's action plan for antimicrobial resistance by reducing cross-transmission of AMR infections in hospitals.

SUPPORTING INDUSTRY

The NML is a partner in the Innovate UK programme ‘Analysis for Innovators’ (A4I). A4I provides companies with access to state-of-the-art measurement and analytical technologies. It focuses on solving measurement problems within existing business to improve competitiveness and productivity.

Due to the success of the programme, the partnership consortium (Innovate UK, NML, NPL, STFC, KTN) was awarded £10M from the government’s Strategic Priorities Fund (SPF) to continue to run A4I Programme for another three years.

This year we have been working with five UK companies to address challenges in healthcare, food and bioscience development. These projects address challenges in quality control to reduce wastage, product improvement to provide regulatory support, and the extension of current products to access new markets.

Projects involving a further eight companies have been approved under the additional SPF funding and will start in early 2019.

> “The A4I project with the NML provided crucial technical validation and has given significant credibility to our novel disruptive technology. It has given us confidence to bid for contracts that we may otherwise have not considered.
>
> Rayne Longhurst,
> Operations Director, AQR

A4I Analysis for Innovators

AQR

Novel solutions for wastewater management are necessary for the UK to meet its sustainability goals, reducing water wastage and reusing resources wherever possible. Air Quality Research Ltd (AQR) developed a chemical-free, energy-saving technology for bacterial control and chemical decontamination, providing safe water for use in the home and industry.

Through our collaboration under A4I they were able to validate their process and further improve the efficiency of their treatment process. As a result AQR is now working on a feasibility study with a major water company to sustainably provide affordable drinking water to small rural communities, improving local regional infrastructure. If successful, this study could lead to significant investment in the business.

Ludger

Simple and complex carbohydrates (glycans) play a major role in the behaviour of biopharmaceuticals and must be well characterised to ensure their safety and efficacy. Glycan standards are a key tool to help with characterisation and quantitation and can provide vital information on the performance of an analytical process. However the complex characteristics of glycans makes their analysis very challenging.

Using our expertise in quantitative NMR (qNMR), we are collaborating with Ludger, a leading provider of standards and technology for analysis of glycans, to develop novel calibration approaches to accurately quantify glycan standards (2D qNMR). This work will allow Ludger to further improve the product specifications of their glycan standards and support their customers that require traceability to the SI for regulatory purposes.

> “The A4I project with the NML allowed us to develop a method that otherwise would have not been feasible. It will ultimately lead to improved product offerings and an expansion of our quantitative product range.
>
> **Jenifer Hendel, Daniel Spencer and Simon Peel, Ludger Limited**

Smith+Nephew

Patients with chronic or acute wounds, such as diabetic ulcers, burns and post-operative wounds, need advanced wound care to help reduce infection and improve healing. With an ageing population that is more prone to chronic illnesses, and where natural healing processes are slower and less efficient, wound care is becoming ever more important.

Under A4I, we are working with Smith + Nephew (S+N), a global medical devices company, to provide high accuracy data to support the development of novel wound treatment products. The project will provide a truly collaborative approach, combing the in-house research capability of S+N with advanced imaging and surface analysis technologies available within the UK’s National Measurement System.

This work will support S+N in their aim to reduce the human and economic cost of wounds, improving patient outcomes and conserving resources for health systems.

> “This programme is genuinely useful for industry and we are very pleased to be a part of it.”
>
> **Paul Gunning, S+N**

HELPING ADDRESS THE GRAND CHALLENGE OF HEALTHY AGEING

Our population is ageing: in the next twenty years, the number of people over 75 in the UK will have increased from 1 in 12 to 1 in 7. A third of those children born today are expected to live to 100. The associated increased incidence in chronic conditions such as Alzheimer's diseases or cancer presents a significant challenge to the health services.

At the NML we are helping to address this challenge by improving the reliability and accuracy of measurements used in clinics and ensuring that emerging therapies and diagnostic approaches are based on sound measurement science. This will help provide the most effective patient care to improve quality of life in the future.

A NEW ROUTE TO ALZHEIMER'S DISEASE DIAGNOSIS

Neurodegenerative diseases are currently incurable conditions that lead to a decline in memory, thinking and language skills often referred to as dementia. Around 50 million people live with dementia worldwide - with one new case every 3 seconds.

Early diagnosis of Alzheimer's disease, the most common form of neurodegeneration, can help patients access effective treatments and sources of support, but studies suggest only half of people with the condition have been diagnosed.

A variety of different metals and metal complexes play a role in the development of Alzheimer's disease and have the potential to be used as clinical biomarkers. However, many of these metals are present only at very low concentrations (part per billion or less) and in different forms in blood or cerebral spinal fluid (CSF). Furthermore, only small amounts of sample are available for analysis in the clinic, presenting a complex measurement challenge.

Using our analysis expertise, we have developed a rapid quantitative method for analysis of multiple metals in small volumes of of human samples using inductively coupled plasma mass spectrometry (ICP-MS). The method has been validated against high accuracy reference methods in inter-laboratory comparison studies of clinical samples performed under a European-funded project (ReMIND). It has the potential to be easily adopted by clinical laboratories and healthcare companies to support reliable, comparable measurements for neurodegenerative disease diagnosis and monitoring.

We are currently working with a pharmaceutical company to extend and enhance this method to improve diagnosis of Wilson's disease, a rare genetic disorder characterised by an accumulation of copper in tissue, and assess efficacy of copper chelating treatment approaches in a clinical trial.

MEASUREMENT TO SUPPORT CANCER TRIALS

Selenium is a trace element with known anti-cancer properties. At certain doses, it has shown promise in enhancing the efficacy of chemotherapy drugs in the treatment of cancer in preclinical studies. However, as some forms of selenium (species) can be harmful, it is important to understand the mechanisms by which they work in order to know which ones can be safely used.

At the NML we have developed a high accuracy method (affinity chromatography inductively coupled plasma mass spectrometry) to quantify different species of selenium (e.g. selenoproteins) in human samples. Using this approach we are working with Waikato Hospital, New Zealand, and other international partners to assess the safety and beneficial effects of different selenium drugs on cancer patients. This is the first human cancer trial investigating the use of selenium.

Our data on the amount of total selenium and different selenium species are being correlated with activity data from other partners against the different drug profiles in this randomised blind study. The initial results are encouraging and scheduled for reporting.

The second phase of this trial, due to start recruiting shortly, will evaluate the most effective selenium drugs in combination with chemotherapy to find the best combination therapy. This will ensure that any cancer treatment improvements using selenium are based on sound measurement science to provide the most effective patient care.

HELPING TO PROTECT OUR ENVIRONMENT

Mercury (Hg) is one of the most toxic metals. To protect human health and the environment from its adverse effects, European and global directives (e.g. Minamata Convention) ensure mercury is closely regulated.

The industrial sector is one of the main causes of mercury pollution, with mercury being released in gaseous form in to the atmosphere. Systems to monitor mercury are installed in stacks and these are calibrated using a standardised mercury solution to give accurate results.

However, little data exists on the elemental purity of the mercury salt used to create these solutions. Even very low level elemental impurities could potentially affect the output of the gas standard generators with time and compromise the fidelity of the monitoring system.

Using our expertise in inorganic purity and speciation analysis, we worked with the Dutch measurement institute VSL to screen the salts being used to develop the mercury standards.

PROTECTING THE SAFETY OF OUR STREETS

Non-laboratory based chemical measurements are important for many sectors, including law enforcement, security, health and food. Testing at the point of need, e.g. at the roadside or on a production line, requires robust, cheap and easy to use instrumentation that is portable.

Advances in technology now mean mass spectrometry does not need to be restricted to the laboratory. We have been working with the instrument manufacturer Waters to develop a prototype ambient ionisation source (atmospheric solids analysis probe (ASAP)) that allows for direct analysis of solid and liquid samples with little or no sample preparation.

Using this source we have developed a method to identify the main components of bulk drug seizures in less than a minute. We have applied this method successfully to a range of sample types, including powders, pills and plant materials.

We are now in discussion with forensics providers to evaluate this instrument for routine drug seizure analysis.

Waters

> “The use of purity data in the calculation of the composition of calibration gas mixtures is an essential element in establishing metrological traceability of the certified gas composition. [The impurities] have an impact on the uncertainty associated with the content of the component.
>
> **Iris de Krom, Scientist, VSL**

SUPPORTING THE BIOPHARMACEUTICAL INDUSTRY

Bio-therapeutics represent the largest growing area of the pharmaceutical sector: estimated to account for approximately 20% of all marketed medicines and around half of all new medicines being approved. However, the process of bringing a bio-therapeutic to market is expensive, time-consuming and high risk, with fewer than 1 in 10 products being successful.

Throughout their development life cycle these bio-therapeutics are continuously monitored to ensure quality and efficacy is maintained.

One of the important characteristics that must be monitored to evaluate stability, potency and immunogenicity is the higher order protein structure (secondary and tertiary) of a bio-therapeutic. Doing this accurately and reproducibly is challenging.

Many different analytical and biophysical techniques of varying complexity, novelty and expense could be employed. However, no guidelines currently exist to help industry determine when different techniques are fit for purpose.

Using our expertise in structural protein mass spectrometry we have been working with industry, academia and the measurement community to address this challenge. We have developed novel protocols that can be used to assess sensitivity of the method to structural changes and benchmark new platforms.

We co-ordinated an inter-laboratory study to evaluate different analysis platforms for their sensitivity to structural changes using an easily accessible model system that we developed and characterised in house. The study included both routine approaches traditionally used by the biopharmaceutical industry (e.g. CE, Raman, AUC) as well as more specialised and emerging approaches (e.g. NMR, HDX-MS, IMS-MS) that could be adopted in the future.

The model system we developed provides a tool to facilitate comparability of structural measurements as required by regulators (ICH Q5E) and improve confidence in the results that are submitted. This will help enhance the quality and safety of biopharmaceuticals, ultimately supporting improved access to novel therapies, reducing healthcare costs and improving patient care.

WORKING ACROSS THE NMS TO DEVELOP METHODS FOR OPTIMISATION OF FORMULATION AND DEVELOPMENT OF BIOSIMILAR STANDARDS

Granulocyte colony stimulating factor (G-CSF) is used to help patients’ white blood cells recover after chemotherapy treatment and reduce infection. The recombinant form of G-CSF (rhG-CSF), i.e. the form produced in a laboratory rather than being animal or human-derived, was one of the first recombinant biologics that was authorised for medical use.

Following patent expiration of the original product (filgrastim), multiple biosimilar versions have been approved for use in the EU. These are highly similar biological products that have been shown to be clinically comparable with the original with respect to quality, safety and efficacy. However, rhG-CSF is a small protein that tends to accumulate and form clumps (aggregates). These aggregates cause decreased efficiency, reduced shelf life and increased immunogenicity of the drug and so it is important to optimise the inactive components that are included with the biologic to stabilise the protein.

We have been working with NIBSC, the UK Designated Institute for biological activity, and University College London (UCL) to understand the effects of different inactive components on the stability of rhG-CSF.

MEASUREMENT FOR THE FUTURE

TOWARDS ELEMENTAL IMAGING OF A SINGLE CELL

The development of novel treatments relies on being able to measure and characterise the medicines accurately, both in their place of manufacture and in our bodies.

Many in-vitro tests are performed on groups of cells, under the assumption that all cells of a particular ‘type’ are similar. However, individual cells within the same population may differ from each other and in how they behave. In order to best understand the efficacy of treatments, it would be advantageous to be able to monitor behaviour within a single cell.

Under an Industrial Strategy Challenge Fund project, the NML has invested in new capability having installed one of the first high resolution inorganic time-of-flight mass spectrometers in the world. Coupled with our fast high-resolution laser ablation technology we have the capability to monitor the distribution of multiple elements, tags or isotopes within a single cell (at 2 µm resolution) in a few minutes.

The increased sensitivity, speed and resolution of this platform will ultimately provide a gold standard for quantitative single cell elemental imaging, allowing us to see how well medicines are performing inside individual cells.

This approach will help clinicians underpin current techniques, such as mass cytometry, inform and validate drug treatment protocols for pharmaceutical companies, and provide evidence for effective targeting of disease.

STANDARDS FOR CELL THERAPIES

We were involved in the development of five new written standards that were released by ISO (International Standards Organisation) to support the production of cellular therapeutic products. These standards are developed by international experts to help encourage innovation and provide solutions to global challenges.

ISO 20391-1:2018 Biotechnology - Cell Counting - Part 1: General guidance on cell counting methods

ISO TS 20399-1:2018 Biotechnology - Ancillary materials present during the production of cellular therapeutic products - Part 1: General requirements

ISO TS 20399-2:2018 Biotechnology - Ancillary materials present during the production of cellular therapeutic products - Part 2: Best practice guidance for ancillary material suppliers

ISO TS 20399-3:2018 Biotechnology - Ancillary materials present during the production of cellular therapeutic products - Part 3: Best practice guidance for ancillary material users *(leading)*

ISO 20387:2018 Biotechnology - Biobanking - General requirements for biobanking

TOWARDS A BETTER UNDERSTANDING OF GENE EDITING

Gene editing technologies such as CRISPR that can rapidly make changes to DNA are starting to revolutionise the field of medicine, particularly for cancer and genetic blood disorders.

When making changes to the DNA sequence, it is vital to understand how accurate and reproducible these changes are, and whether unintended areas of the DNA are being affected. These so-called “off-target effects” could have wide reaching health consequences for the patients.

We are using our expertise in digital PCR to develop novel methods to quantify the efficiency of gene editing technologies and to screen for off-target events. These methods, developed under an Industrial Strategy Challenge Fund project, will ultimately be used to validate different gene editing approaches and help support their adoption by industry.

KNOWLEDGE TRANSFER & DISSEMINATION

For over 20 years we have provided a programme of courses focused on laboratory quality assurance to help skills development and ensure laboratories across the world meet accreditation and regulatory requirements.

DELEGATES TRAINED | **370** ACROSS **26** COURSES

SECTORS | CLINICAL, ENVIRONMENT, PHARMACEUTICALS, CHEMICALS, FOOD AND BEVERAGES, FORENSICS, UTILITY SERVICES, ACADEMIA

OVER 95% | OF RESPONDENTS FEEL OUR TRAINING COURSES MEET THEIR EXPECTATIONS

The courses help develop the analytical measurement science skills required within the UK and support industry and healthcare address evolving regulatory and accreditation requirements. They include topics such as evaluating measurement uncertainty, designing effective experiments, and statistical tools for analytical scientists.

Our courses consistently receive excellent feedback from delegates and we have a high level of repeat customers.

Details of all our training programmes are available at **www.lgcgroup.com/training**.

> Great course, necessary for people needing accurate information on what is required for validation, especially for UKAS accredited testing.

Training course delegate

GOOD PRACTICE GUIDE FOR ISOTOPE RATIO MASS SPECTROMETRY

The isotopic composition – the ratios of the stable isotopes of elements such as 2H/1H or 13C/12C – provides an isotopic fingerprint of a material, which can reveal information about its geographical origin, how it has been processed or manufactured or when it was produced. They can be used to detect testosterone doping, identify counterfeit pharmaceuticals, or feed in to climate models used to determine government economic policies.

Regardless of the application area, good practice is essential to ensure the quality of isotope ratio data is fit-for-purpose and any conclusions drawn from the interpretation of results are sound. In collaboration with the NML, the Forensic Isotope Ratio Mass Spectrometry (FIRMS) Network recently updated their highly regarded Good Practice Guide for Isotope Ratio Mass Spectrometry (IRMS).

This edition reflects the significant instrumental developments in the field over the last seven years. It includes further guidance on fundamental measurement science principles such as traceability and measurement uncertainty estimation and has already been referenced many times.

SUPPORTING THE CATAPULT CENTRES

The Cell and Gene Therapy Catapult is a centre of excellence in innovation, with the core purpose of building a world-leading cell and gene therapy sector in the UK as a crucial part of a global industry. Reliable measurements are crucial to underpinning this aim. The NML has delivered on-site courses covering method validation and statistics to support staff in ensuring the validity of their measurement results.

SKILLS FOR INDUSTRY

CAMS
Community for Analytical Measurement Science

We are a partner in CAMS (Community for Analytical Measurement Science), an industry-led initiative to support the provision and development of professional training programmes to provide UK industry with the skilled scientists they need.

In addition to helping to establish the initiative, we provide ongoing Secretariat support to CAMS, part-funded by the RSC Analytical Chemistry Trust Fund.

CAMS is made up of a virtual centre for post-graduate students (Measurement Science Research Institute, MSI) and a chemical and bio-analytical training institute (BEAM). Ahead of the formal launch in 2019, there is already significant financial support pledged from industry alongside leveraged funding from universities for research positions from studentships to Chairs.

As part of our NML activities to provide ongoing training material for BEAM, we are collaborating with Learning Science, a Bristol-based company producing interactive learning resources for the university sector, to provide training material for chemists and bio-analysts working in regulated laboratories.

The pilot project, funded by BEIS (Department for Business, Energy and Industrial Strategy), will initially focus on basic laboratory skills such as weighing, pipetting, volume measurement, solution preparation, dilution and centrifugation.

Once developed and evaluated by practicing analysts, this new material will help laboratory practitioners develop the skills they need to improve the quality of analytical measurements. It will provide evidence of competence and ultimately improve business performance through increased efficiency, reduction of costs and avoidance of risks of passing on incorrect results to customers.

SELECTED PUBLICATIONS

The quality and credibility of our science is demonstrated in part through our publications in peer-reviewed journals. This year, experts within the NML published 30 scientific papers. Here is a selection:

Dunn PJH & Carter JF (eds). Good practice guide for isotope ratio mass spectrometry, 2nd Edition. FIRMS. ISBN 978-0-948926-33-4

Ellison SLR & Botha A. Principles for the assessment of homogeneity and stability in the new ISO Guide 35:2017. Accred Qual Assur 23: 47. DOI:10.1007/s00769-017-1293-5

Gale D et al. Development of a highly sensitive liquid biopsy platform to detect clinically-relevant cancer mutations at low allele fractions in cell-free DNA. PloS One 13:3, e0194630. DOI:10.1371/journal.pone.0194630

Koller D et al. Analysis of soluble or titanium dioxide derived titanium levels in human whole blood: consensus from an inter-laboratory comparison. Analyst 143:5520-5529. DOI:10.1039/C8AN00824H

Malinovksy et al. Development and characterisation of new glycine certified reference materials for SI-traceable 13C/12C isotope amount ratio measurements. J Anal Atom Spectrom 34:147-59. DOI: 10.1039/C8JA00281A

Shard AG et al. Measuring the relative concentration of particle populations using differential centrifugal sedimentation. Anal Meth 10:2647-57. DOI: 10.1039/C8AY00491A

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OUR PEOPLE

Vicki Barwick was elected as Vice-Chair of Eurachem. This is a two-year term running until 2020, after which she will become the Chair.

Philip Dunn was involved in establishing the newly formed CCQM Working Group on Isotope Ratios, recognising our expertise in this area, and will now represent the NML on this group going forward as the Vice-Chair.

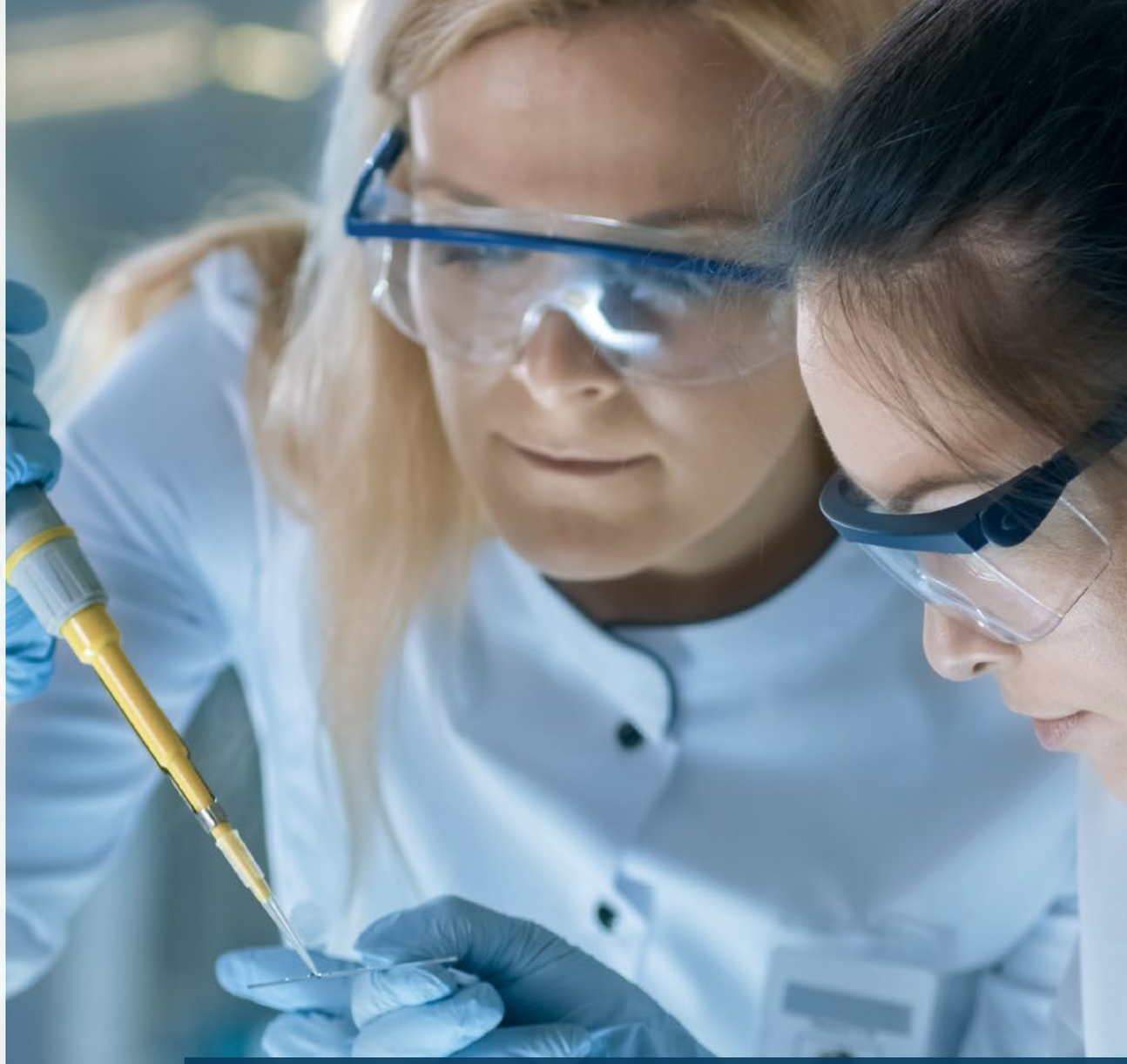
Heidi Goenaga-Infante was one of three leading European scientists short-listed for the European Award for Plasma Spectrochemistry 2019 based on her continuous contributions to the field.

Dmitriy Malinovskiy was selected again this year as one of the top 10 worldwide reviewers of the Journal of Analytical Atomic Spectrometry (JAAS) due to the high quality of his reviews.

Julian Braybrook, Director of Measurement Science at the NML, was appointed to the position of Government Chemist.

Frank Torma was awarded his PhD from the University of Reading. His PhD work was on the SI traceable quantification of clinically relevant proteins using mass spectrometry.

OUR PEOPLE
80 SCIENTISTS
75% PhD



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measurement@lgcgroup.com
training@lgcgroup.com
+44 (0)20 8943 7393
+44 (0)20 8943 7631

LGC, Queens Road,Teddington, Middlesex TW11 0LY, UK
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