



NML at LGC response to COVID-19 pandemic



Throughout the pandemic we have kept essential laboratories open and re-scoped work to directly support the UK and the global measurement community response to the COVID-19 pandemic by:

Leading the way in international standardisation

Supporting the standardisation of viral diagnostics

The International Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (**CCQM**)- Nucleic Acid Analysis Working Group (NAWG) have developed a reference measurement procedure through an inter-laboratory study for **SARS-CoV-2 genome measurement under an accelerated timeframe** to support COVID-19 molecular diagnostic testing. This study was led by the **National Measurement Laboratory (NML) at LGC**, as part of its Department of Business, Energy and Industrial Strategy (BEIS) functions, and supported by the National Institute of Biological Standards and Control (NIBSC) and the American and Chinese national measurement laboratories. It measured the genes targeted by diagnostic tests to SARS-CoV-2, using materials developed in the UK and China, and involved twenty one national measurement laboratories and approved guest laboratories from sixteen countries. The study demonstrated that highly accurate measurements of the amount of the SARS-CoV-2 viral RNA can be achieved worldwide using reverse transcription PCR (RT-dPCR) without calibration. It represents the most comprehensive example of highly reproducible measurement of RNA and enables globally standardised testing by assisting diagnostic manufacturers with test development and providing quality assurance of routine COVID 19 testing.

The availability of calibration-independent reference measurement procedures have far wider implications as they can provide a global foundation for rapid implementation of diagnostic standards that are able to be tailored to a wide area of applications, for example in future pandemics, cancer testing and antibiotic resistance.

In our role as nominated **expert laboratory for external quality assurance provider INSTAND eV**, we have applied the international method to assign values for virus quantification together with the German and American national measurement laboratories. Current activities relate to value assignment and evaluation of homogeneity for PT schemes conducted in March, June and November 2020 (600+ participants).

The techniques being developed in the **NML-led EMPIR project SEPTIMET** (Metrology to enable rapid and accurate clinical measurements in diagnosis and acute management of sepsis) have application to the COVID-19 pandemic as some of the measurement challenges are shared with those for managing COVID-19 patients; as such, the project now includes the virus as one of its models to investigate whole genome sequencing and the evaluation and characterisation of molecular targets in clinical samples using alternative molecular methods including Loop mediated isothermal amplification (LAMP) assays.



Supporting the standardisation of serology diagnostics

We are participating in a second **CCQM inter-laboratory study** together with other international national measurement laboratories for antibody characterisation to support the development of COVID-19 serological tests, as well as assisting in the development of complementary reference materials to underpin the accuracy of these tests.

International documentary standards and guidance

As an early partner in the establishment of the “**Coronavirus standards working group**” (based in USA with global participation), expert input is being provided to international guidance on assay design and standards assessment.

A recently completed European (EMPIR) project for improved bio-analytical measurements led by the NML, has helped develop three international (**ISO standards**) regarding the counting of biological entities, **important for diagnosing respiratory infections and identification of microbial pathogens**. One of these (ISO 20395:2019 Requirements for evaluating the performance of quantification methods for nucleic acid target sequences – qPCR and dPCR) has been made [freely available by ISO](#) to support the development and implementation of effective COVID-19 testing. The standard has been used in the implementation of quality assurance for UK COVID-19 field-testing laboratories. The European Commission also [highlighted](#) this work as one of their research and innovation initiatives to help tackle the spread of coronavirus and preparedness for other outbreaks.

We are representing the UK in the ISO/TC 276 and ISO/TC 212 joint working group and drafting committee for the technical specification document ‘Quality Practice for detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by nucleic acid amplification methods.’

World Health Organisation (WHO) international reference standards

We participated in the value assignment of the international assessment of the **WHO SARS-CoV-2 international standard** released January 2021.



Supporting the Medicines and Healthcare products Regulatory Agency (MHRA)

To support **emergency COVID-19 medicine testing requests**, our MHRA Laboratories Team has established a new office and laboratory footprint, allowing distinct, socially distanced bubbles of operation. In this way, the Team **maintained stocks of** up to 134 priority **British Pharmacopoeia Certified Reference Standards** necessary for medicine testing of COVID-19-related therapeutics.

Supporting the NHS and PHE nationally

As well as providing regular ad hoc advice to the NHS around validation of specific test method performance, the NML and Public Health England (PHE) have been working together to support technical input into the Department of Health and Social Care (**DHSC**) **Viral Technology Group** to evaluate the performance of commercial COVID-19 molecular diagnostic viral test approaches used within the NHS and Lighthouse laboratories.

We are part of the **NHS Test and Trace Mass Spectrometry Pilot Study**, assisting in the translation from academia to NHS clinical laboratory of a fit-for-purpose diagnostic method for COVID-19 testing.

Advising the NHS locally

Collaborating with local UK NHS hospitals and testing laboratories (including **Great Ormond Street Hospital (GOSH)** and **Health Services Laboratory**), we have assisted in the clinical development and utility of COVID-19 testing to ensure the robustness of different assays being applied to the increased volumes of patient samples at the front line.

The NML is expanding its links with GOSH to investigate viral load as part of the above NML-led **EMPIR project SEPTIMET**.

Assisting other national centres of excellence

The NML has supported the **Welcome Trust Sanger Centre** sequencing of the genomes of SARS-CoV-2 virus from patients, providing advice on sample handling and control materials to ensure the confident application of their sequencing pipelines.



Collaborating with academics

We are partners in **joint collaborative academic research proposals** to use our mass spectrometry and molecular biology resources and expertise to help develop improved molecular and antibody testing for the COVID-19 pandemic.

The Mass Spectrometry COVID-19 coalition, a global initiative led by the University of Manchester, UK, was set up to inform serological testing, support vaccine and therapeutic development (mapping viral proteins and their interactions) and develop methods to determine disease prognosis and the lifetime of infectious particles in the environment.

The **COVID-19 National Diagnostic Research and Evaluation Platform (CONDOR) initiative**, funded by the National Institute for Health Research (NIHR) and UK Research and Innovation (UKRI), has created a national route for evaluating new diagnostic tests in hospitals, GPs and care homes. Led by Manchester University NHS Foundation Trust (MFT) and the University of Oxford, in collaboration with four NIHR Medical Technology and In vitro Diagnostics Co-operatives (MICs), CONDOR is one of a number of COVID-19 studies given **urgent public health research status**. As the NML, we are supporting the independent validation of molecular point of care tests under consideration.

Linked to the CONDOR initiative, we provided control materials for the Liverpool School of Tropical Medicine to evaluate their molecular diagnostic assays.

Helping industry

We continue to work with industry on **critical and emerging businesses needs** where chemical and bio-measurement expertise is required to support their activity in response to COVID -19, e.g. the production of PPE, alcohol hand wipes and diagnostic kit development.

We are a partner in the **Measurement for Recovery (M4R) Programme** that brings together the experts and specialist facilities from the UK National Measurement Laboratories to help solve measurement issues in innovative ways to help UK industries in their recovery from the COVID-19 pandemic. The NML are specifically working with a company to accelerate the development of their SARS-CoV-2 rapid antigen test, one of the twenty finalists in the multi-million XPRIZE Rapid COVID Testing.

We are a member of the UK hospitality industry's [Safe to Trade Scheme \(STTS\) Governance Board](#), launched in direct response to the COVID pandemic to help instil consumer and worker confidence so that businesses can re-open and trade safely by complying fully with the government recommendations. Hundreds of venues have already signed up to the Scheme, with many more joining on a weekly basis.

As Project Leader for the **Food Authenticity Network** (www.foodauthenticity.global) we were instrumental in publishing a **COVID-19 Resource Base** to help businesses secure their food supply chains by mitigating food fraud. This attracted substantial trade magazine interest and coverage. In addition, the [Food Authenticity Network \(FAN\)](#) conducted an independent verification assessment of circulating data showing a “dramatic increase in food fraud since COVID-19 Outbreak”. The study, [published](#) in IFST's Food Science & Technology journal in December 2020, allayed any substantial concern but indicated that the true impact of the COVID pandemic on the incidence of global food fraud will not be known until full resumption of regulatory surveillance world-wide.

Broader communications/publications

We provided scientific content and consultation on script for a **TEDEd Animation** on [“How do virus tests actually work?”](#)

We contributed to a **Royal Society policy briefing** on COVID-19.

We provided joint opinion and correspondence pieces on [“Diagnostic tests for covid-19—improving accuracy and global harmonisation”](#) and [“The COVID-19 MS Coalition—accelerating diagnostics, prognostics, and treatment”](#) published by the **British Medical Journal** and **The Lancet** respectively.

We authored the invited manuscript “Novel detection methods for SARS-CoV-2 infection and considerations for their translation to routine use”, in a special issue of **Current Opinion in Pulmonary Medicine Journal**.

We authored the publication [“Cautionary Note on Contamination of Reagents Used for Molecular Detection of SARS-CoV-2”](#) in **Clinical Chemistry**.

We contributed to the publication “Comparison of SARS-CoV2 N gene real-time RT-PCR targets and commercially available mastermixes”.

