NAVIGATING THE POST-PANDEMIC LANDSCAPE: NML'S USE OF METROLOGY

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The National Measurement Laboratory (NML) at LGC is a strategic national asset that provides a unique national capability for the UK, providing further confidence in the UK's science and technology capabilities, and is essential for advancing measurement science, ensuring precision and accuracy in bioanalytical testing in the UK and worldwide. During the COVID-19 pandemic, NML's expertise was pivotal in enhancing diagnostic test accuracy and laying the foundation for a sustainable UK framework for future pandemic preparedness. This framework guarantees the reliability of diagnostic tests, enabling informed public health decisions.

THE CRUCIAL ROLE OF BIOANALYTICAL BREAKTHROUGHS IN HEALTHCARE ADVANCEMENTS

The advances in healthcare over the last half century have been unparalleled, with major improvements in mortality and morbidity associated with conditions ranging from cancer and cardiovascular diseases to infectious diseases. Many of these breakthroughs have needed cutting-edge advances in bioanalytical tests to provide accurate information on the physiology, immunity, or genetics to aid in diagnosis, prognosis and longitudinal monitoring of disease progression and treatment response.

The need for bioanalytical technologies was highlighted during COVID-19. How could governments have responded to COVID-19 without genetic sequencing, PCR, and later, lateral flow tests? Yet this episode also highlighted the critical need for precision and accuracy in healthcare testing. As bioanalytical technologies provide previously unknown clinical and epidemiological information across various diagnostic challenges, the community becomes more dependent on the outcomes of the tests in decision-making. Consequently, it is paramount that the methods are known, and can be demonstrated, to be working within specified parameters to address challenges from antimicrobial resistance to precision medicine for patient benefit.

NML'S METROLOGY ROLE:

The NML is the UK's designated institute for chemical and bio-measurement and, as a national laboratory and PSRE (based in a private limited company), is a crucial part of the UK National Measurement System. We provide high-quality world-leading science, to solve measurement problems and provide the resilient measurement infrastructure

needed to support government, healthcare, industry and protect consumers within the UK, as well as representing the UK's measurement interests internationally. We address emerging challenges in measurement science, supporting businesses to innovate more effectively and with less risk – through the application and translation of fit-for-purpose measurement solutions and the provision of standards that underpin complex measurements – and so fostering economic growth.

OUR PANDEMIC RESPONSE

Over the last fifteen years, we have led the development of a global framework for biological measurement quantification. Through UK government funding in our national role, combined with additional leveraged income through European projects (Horizon 2020), we have developed advanced nucleic acid measurement capabilities and expertise within the UK, establishing it as a leading measurement institute in supporting pathogen analysis. Our strategic role has been pivotal in improving the comparability and traceability of infectious disease diagnostics, informing clinical best practice, supporting molecular diagnostic accreditation, and contributing to international standards.

As a result, we were well-positioned to respond to the COVID-19 pandemic, quickly developing reference methods required to support accurate molecular detection and providing independent advice.[1] We collaborated with government, industry, and academia to establish a national testing programme, founded on reliable chemical and biological measurement science.

During the pandemic, the need for clear technical guidance in developing in vitro diagnostic tests for SARS-CoV-2 detection became paramount. Representing BSI on the International Organization for Standardization (ISO) diagnostic committee in January 2021 highlighted the potential threat variants of concern (VoC) could have on diagnostic testing. We played a central role in drafting requirements to screen for VoC in collaboration with the Medicines and Healthcare products Regulatory Agency's (MHRA)[2].

Through collaboration with MHRA we developed Target Product Profiles (TPPs) for diagnostic tests. These profiles guide manufacturers in test development, considering factors like usage, location, and result application (e.g., contact tracing or isolation decisions). We ensured TPPs had accurate terminology and clear technical directions, ensuring effective and scientifically rigorous SARS-CoV-2 diagnostic tests. This emphasized the importance of precise early diagnostics in pandemic management and provided guidance for COVID-19 in vitro diagnostic manufacturers[3].

In April 2020, over 480 laboratories joined one of the first external quality assessment schemes (EQAs), a vital milestone. For the first time, laboratories could validate the fast-developed independent methods. Leveraging our expertise based on our experience, we characterised materials with high accuracy. A follow-up study assigned virus numbers to these materials, establishing benchmarks for laboratory competency and test reproducibility[4].

NML, in collaboration with MHRA and NIM China, led global comparison studies, including a rapid reference measurement pilot for COVID-19 (CCQM NAWG P199b) to standardise molecular diagnostics. This study demonstrated method comparability for end-user testing at an unprecedented pace in the measurement community.

Despite these achievements, it's essential to stress the ongoing need for improving testing efficiency and accuracy. Our extensive work during the COVID-19 pandemic underscores the importance of integrating national and international measurement expertise into pandemic preparedness. A comprehensive reference system, encompassing both quality control materials and reference methods, should be a vital part of rapidly deploying diagnostic tests in response to new outbreaks. Enabling comparisons across various approaches through a centralized, accessible process will benefit end-users, highlighting the importance of a cohesive and standardized response in future health emergencies.

LEARNING FROM THE PANDEMIC: THE 100-DAY MISSION, CCQM ROADMAP AND GLOBAL HEALTH STRATEGY:

The pandemic highlighted the crucial role of diagnostics in identifying and managing health crises. It became clear that early and robust diagnostic capability was key to managing the disease.

In response to the Covid-19 pandemic, the 100 Days Mission[5] was published, an ambitious initiative produced through collaboration between global experts. Its main objective was to develop safe, effective, and affordable rapid diagnostics, therapeutics, and vaccines within 100 days of a major outbreak. Building robust, sustainable resources for rapid activation and implementation of diagnostic measures in response to emerging health threats is essential to achieving this target.

Working closely with the measurement community, and national and global policy and healthcare officials who were on the front line of managing national responses to COVID-19, we led the development of the CCQM Pandemic Roadmap[5]. This roadmap sets out recommendations for specific measurement interventions to enable a rapid response and enhance clinical outcomes, providing globally accepted baseline measurements for policy decisions in future infectious disease outbreaks.

It focuses on a deep understanding of pathogens, the standardization of test requirements for in vitro diagnostic devices, and the proactive development of diagnostics, therapeutics and vaccines (DTVs). These measures are critical for effective pandemic management, highlighting the roadmap's comprehensive approach to public health crises.

EMBRACING COLLABORATION:

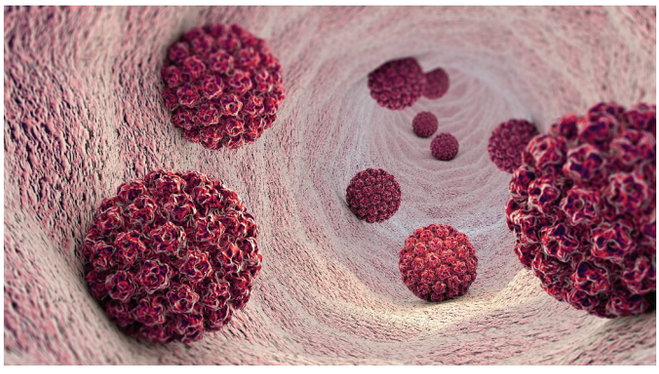
Central to our work is the establishment of a multidisciplinary expert community in the diagnostic space in the UK. An interconnected measurement system is vital for advancing global health responses, ensuring diagnostic accuracy, supporting regulatory compliance, and enhancing public health management. Collaboration in measurement science is instrumental in achieving the objectives of the CCQM Roadmap and the 100 Days Mission, ultimately improving pandemic response strategies.

THE PANDEMIC PARLIAMENTARY EVENT:

As part of our collaboration initiative, we hosted a Pandemic Preparedness Event at

Parliament in October 2023. The event emphasized our dedication to the 100 Days Mission and its role in implementing post pandemic responses. Hosted in the House of Commons and chaired by Stephen Metcalfe MP, it featured advancements in diagnostic testing from ourselves, MHRA, UKHSA, NHS laboratories and others, and reinforced the UK's leadership in this field.

The discussion stressed diagnostics' pivotal role in addressing various health challenges, especially in pandemic preparedness based on COVID-19 lessons. It emphasized their importance in dealing with infectious diseases, antimicrobial resistance, precision medicine, and cancer



detection. However, diagnostics, despite their cost-effectiveness and early detection benefits, often receive less funding and policy attention than therapeutics and vaccines. Clear, consistent, ambitious government policies are crucial to boost confidence in the UK diagnostics industry, promote investments, ensure sector stability, and maximize its impact.

The discussion concluded with a forward-looking perspective on how the framework, spearheaded by the UK, is being implemented to ensure timely access to quality-assured diagnostic tests for future infectious diseases.

Following on from this event, the NML is continuing to work across the diagnostics, regulatory and policy communities to raise the profile and importance of diagnostics further.

References

1 https://www.lgcgroup.com/pandemic-preparedness/

2 ISO/TS 5798:2022 - In vitro diagnostic test systems — Requirements and recommendations for detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by nucleic acid amplification methods

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5 https://www.bipm.org/en/-/2022-06-16-ccqm-pandemic-roadmap