EPBS Position paper

COVID-19 Pandemic and the Role of Biomedical Scientists

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Introduction

Although a pandemic has been predicted several times over the past decades, little was done to prepare for it in Europe. Now we are paying the price. A worldwide outbreak with many sick people, many hospitalizations and, tragically, many deaths. Management of this pandemic has challenged Governments, Health Authorities and the Medical and Nursing professions. One other profession, normally hidden from public view, the Biomedical Scientist, has stepped into limelight and their contribution to the diagnosis and monitoring of the progression of this disease has been, and will remain critical, for SARS-CoV-2 management. Without robust testing systems and a European wide coordinated approach to testing regimens the resumption of normal life and commerce will be delayed.

The emergence of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection presents the greatest health challenge to Europe and to the rest of the world. It is clear the virus can, and will, mutate to maintain infectious advantage.[1] The response to this virus needs to be consistent at a national, regional and global level. It needs to be informed by, and adapt to, the evolving evidence and science. The global response has been innovative with rapid development and deployment of testing platforms and novel vaccines that would normally take many years to bring to market. These programs of testing, tracing, and vaccination are proving effective but, as the virus continues to evolve, full immunity has not been established. Indeed, some seven months post rollout of comprehensive vaccination programs evidence of breakthrough infection is emerging.[1] It is likely that there will be a continued need to provide testing services for both symptomatic and asymptomatic cases, for contact tracing, to monitor the mutations of the virus and to establish immunity to permit normal life to be re-established safely.

This paper, prepared by the European Association for Professions in Biomedical Science (EPBS), outlines the considerations required for provision of safe testing for SARS-CoV-2 within Europe. It is not a scientific treatise rather a discussion paper for European decision makers, outlining considerations, to assist them forge the right course. In this regard it is important that there is a coordinated European response from all nations within Europe.

Through the course of COVID-19 infection, viral replication, immune response, and inflamma-

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tory outcome are dynamic events that can change quickly, causing different outcomes so it´s very important to use the most appropriate laboratory diagnostic tests for the situation.

Clinical Diagnostic Testing Guidelines

Traditionally clinical laboratory diagnostic tests are provided in a clinical laboratory by scientists, qualified, trained and competent in the analysis. Point of care testing may also be used in a hospital or doctor office setting to provide rapid analysis without the benefit of scientific expertise. Patients with chronic diseases, such as diabetes, may also undertake self-testing. Irrespective of the setting where testing is provided the same guiding principles must apply for both patient safety and quality health outcomes:

- The testing method and equipment used must be fit for the purpose.
- The individual undertaking the test must be trained in how to do the test correctly using the equipment.
- There must be appropriate quality assurance of the entire testing process.
- There must be traceability from patient to result.
- There must be an appreciation of the factors that can influence the test.

Clinical diagnostic laboratories work within a quality management system, many are accredited to the International standards ISO 15189. The standard ISO 17025 attests to the quality of point of care testing systems.

The profession of Biomedical Scientist is regulated within Europe and this confirms that the scientists undertaking the testing in laboratories have the knowledge, skills and competencies to verify the testing system, undertake the analysis and ensure the results are fit for purpose.

There are 3 phases for testing: pre-analytical, analytical and post-analytical.

- **Pre-Analytical** refers to the steps in patient preparation for the test, the correct sampling, sample identification and transport to the testing area. Pre-analytical manipulation of the sample prior to its analysis may also occur.
- **Analytical** refers to the testing system itself; the choice of method, its verification quality assurance and performance
- **Post-Analytical** refers to how the result will be interpreted which must consider the patient clinical details in addition to an understanding of the limitations of the testing process.

The Biomedical Scientist has a major role in each of these phases, either through direct action or the provision of advice.

Pre-Analytical Phase: Sample Collection

SARS-CoV-2 is a respiratory virus. The samples used for testing are either a combination of a throat swab and nasopharyngeal swab or a nasopharyngeal swab alone. The quality of the final analytical result is dependent on the quality of sample submitted for testing. The best analytical method will not produce the correct result unless the sample is fit for testing. It therefore stands to reason that those collecting the specimen are appropriately trained.

Given the contagious nature of the virus it is important that the staff collecting the sample are trained properly and equipped with the appropriate personal protective equipment. Correct sampling of a nasopharyngeal swab is not easy. The swab must be inserted in through the nasal cavity until it reaches the nasopharyngeal area. Once there it must sweep the area to obtain the sample. The sample must be uniquely labelled with a combination of patient and sample identifiers. Each sample taken from an individual must be uniquely identifiable. This unique identifier must follow the sample from collection through testing and reporting to contact tracing. The sample transport medium must be appropriate for the test method being used. The sample must be analysed within a prescribed time from the time of collection to completion for the result to be valid. It is important that all material used in the collection of samples are correctly disposed of in accordance with bio safety regulations.

Staff trained in specimen collection are best placed to collect these samples from patients such as Doctors, Nurses and Biomedical scientists. If other groups, or indeed individ-

uals, are drawing samples they should be trained by competent staff, either directly or via viewing material placed online by the World Health Organisation (WHO) and others via YouTube.

Analytical Phase

The choice of analytical method and setting is a critical step in provision of a testing service. In Europe the *In Vitro* Diagnostic (IVD) manufacturers must validate methods and ensure their 'conformité européenne' (CE) marking is acceptable. This validation ensures traceability of testing components to a standard.

Within the testing centre the method must be fit for purpose. In choosing the method the Biomedical Scientist must consider:

- The purpose of testing: screening or diagnostic.
- The volume of specimens to be tested which may dictate the testing methodology and platform to be used.
- The turnaround time required for the result to be available.
- Disease prevalence.
- The skill of the biomedical scientist or other tester required for testing.

The manufacturer validated method must then be verified for use in the diagnostic setting using the equipment and staff who will perform the test. In addition, the sample matrix must be considered. Can the sample be analysed from any transport medium or must a specific matrix be used?

The specific knowledge skills and competences of a Biomedical Scientist are required to ensure that the testing systems are verified as fit for purpose in a given testing environment. In assessing any testing platform and method for use consideration must be given to many factors:

- **Precision** - The reproducibility of testing method. If the same sample is measured repeatedly, how likely is it that the same result will be achieved.
- **Accuracy** - How close is the reported result to the correct or true result? This considers the systematic error of the analysis.
- **Uncertainty of Measurement** - No testing is exact. A measurement result is only complete if it is accompanied by a statement of the uncertainty in the measurement. Measurement uncertainties can come from the measuring instrument, from the item being measured, from the environment, from the operator, and from other sources. Such uncertainties can be estimated using statistical analysis of a set of measurements and using other kinds of information about the measurement process.[2]

Precision, accuracy and uncertainty of measurement are a function of a combination of the robustness of the analytical method employed, the instrumentation and the competence of the analyst. The most reliable results are obtained when analysis is performed by Biomedical Scientists rather than by others who are not specialists in this area.

Quality Assurance

All clinical diagnostic analysis must be subject to quality assurance. Within clinical diagnostic laboratories this can be broken down into internal quality control and external quality assurance.

Internal Quality Control (IQC)

This is a process whereby the same sample is analysed multiple times, daily with each batch of tests or at defined intervals. The same result should be achieved within an agreed tolerance or standard deviation from the mean. This confirms that a given testing process operates satisfactorily and provides assurance regarding the method, instrumentation and testing personnel.

External Quality Assurance (EQA)

This brings IQC to a different level comparing results from a testing centre to external peers. This confirms consistency of results across testing platforms, testing centres and countries.

There are two major method options for measurement of SARS-CoV-2 commonly known as polymerase chain reaction (PCR) and antigen (or lateral flow) testing. The choice of analytical method must take into consideration the factors outlined above as well as the disease prevalence. It is also clear that

whatever testing methodology is used that the detection and management of this disease is a public health issue, both nationally and globally. Therefore, all testing systems must have a clear reporting route to public health for case management and contact tracing.

Post-Analytical Phase: Interpretation

Interpretation of results of analysis is not straightforward. It is dependent of the capacity of the analytical method to detect the disease and the prevalence of the disease in the population.

The following must be considered.

- **Sensitivity.** The ability of the test to identify those with the disease
- **Specificity.** The ability of the test to identify those without the disease
- **Predictive Value.** This is the chance that a positive test result indicates disease, and a negative result indicates absence of disease. These values are based on a combination of the sensitivity and specificity of the testing method along with the prevalence of the disease in the population

Results of analysis for SARS-CoV-2 should be reported as 'Detected' or 'Not Detected'. Each of these results must be interpreted considering the clinical presentation of the individual. It is most important that it be understood that a 'Not Detected' result is not synonymous with 'absence of infection'. It may be that the sample was incorrectly collected, transported, or analysed. It may also be that the sample was collected too early in the infection life cycle.

Choice of Analytical Method for Detection of COVID-19

The pace with which analytical methods were developed for SARS-CoV-2 (COVID-19) was remarkable. Scientists all over the world worked cooperatively to identify the genetic material and share primers to develop robust molecular testing methods. This, perhaps, led to the impression that this is easy to do. It is not. There are, essentially, two method types for detection of the virus. The first method detects the presence of viral RNA and the second detects the presence of viral antigens. In addition, there are antibody tests which detect the immune response to the infection.[3]

Detection of Viral RNA

Viral ribonucleic acid (RNA) can be detected using nucleic acid amplification (NAAT) methods. NAAT detect genetic material (nucleic acids). NAATs for SARS-CoV-2 specifically identify the RNA sequences that comprise the genetic material of the virus. NAAT first amplifies (make multiple copies) of the virus's genetic material. Amplifying the nucleic acids enables NAATs to detect very small amounts of SARS-CoV-2 RNA in a specimen, making these tests highly sensitive for diagnosing COVID-19. The most common NAAT used in diagnosis is the reverse transcriptase polymerase chain reaction or RT-PCR, typically referred to as a PCR test. Optimal diagnostics consist of a NAAT assay with at least two independent targets on the SARS-CoV-2 genome.

PCR testing is the method generally employed in clinical diagnostic laboratories. Methods have been developed by the IVD manufacturers to run on large, automated platforms capable of analysing several thousand samples per day. The genetic material must be extracted from the virus, mixed with primers to facilitate the amplification of the target nucleic acid sequences and then subjected to the amplification process with a detection system to identify the presence of the amplified target. There are smaller, semi-automated platforms which run nucleic acid extraction and the amplification as separate processes. These platforms can process from 50 to 500 specimens daily depending on the configuration of the analyser. The process of sample preparation through extraction, amplification and detection can take up to 6 hours. Typically, these automated methods are interfaced to laboratory information systems facilitating the logging and tracing of specimens from receipt to the final report. Compiled reports can be sent directly to public health disease surveillance systems for case management and contact tracing.

Rapid PCR methods are available in clinical laboratories where a result can be available within one hour. Some of these analysers are sufficiently portable to be used in the field for

outbreak management or where there are high risk individuals who are resistant to attending at large sampling centres. The cost per test of the sample analysis varies. The rapid detection PCR tests can cost between €50 to 100 per test whereas the automated platforms can run at less than €20 per test.

Detection of Viral Antigen

These are commonly referred to as lateral flow tests (LFT) or rapid antigen tests (RAT). With a COVID-19 LFT, a nasopharyngeal sample is placed on a small absorbent pad, which is then drawn along the pad via a capillary line to a strip coated with antibodies, which bind to SARS-CoV-2 proteins. If these proteins are present, this will appear as a colored line on the test, indicating infection. Results are typically available within 15 minutes.

The arrival of RATs suggested that testing could be decentralized and devolved to work places, schools, sports venues and even homes. While performance of the test may be apparently simple the same attention to detail is required. The sample must be correctly collected and identified. The pre-analytical manipulation of the sample must be performed correctly. All individuals that are in contact with the samples must be provided with, and wear, personal protective equipment. Sample manipulation should be performed in a safety cabinet with all materials disposed of in accordance with biosafety requirements.

The sensitivity of RATs is variable. This variability depends on the specific formulation of the test kit and the operator competence. The World Health Organization (WHO) offers clear guidance on their use.[4,5] The minimum performance requirements of ≥80% sensitivity and ≥97% specificity compared to a NAAT reference assay are required before a RAT can be used to diagnose SARS-CoV-2 infection in a range of settings where NAAT is unavailable or where prolonged turnaround times preclude clinical utility. Tests should only be carried out by trained operators.

A Cochrane review of the use of RATs published in March 2021 concluded: *"Antigen tests vary in sensitivity. In people with signs and symptoms of COVID-19, sensitivities are highest in the first week of illness when viral loads are higher. The assays shown to meet appropriate criteria, such as WHO's priority target product profiles for COVID-19 diagnostics ('acceptable' sensitivity ≥ 80% and specificity ≥ 97%), can be considered as a replacement for laboratory-based RT-PCR when immediate decisions about patient care must be made, or where RT-PCR cannot be delivered in a timely manner. Positive predictive values suggest that confirmatory testing of those with positive results may be considered in low prevalence settings. Due to the variable sensitivity of antigen tests, people who test negative may still be infected. Evidence for testing in asymptomatic cohorts was limited. Test accuracy studies cannot adequately assess the ability of antigen tests to differentiate those who are infectious and require isolation from those who pose no risk, as there is no reference standard for infectiousness. A small number of molecular tests showed high accuracy and may be suitable alternatives to RT-PCR. However, further evaluations of the tests in settings as they are intended to be used are required to fully establish performance in practice."* [6]

While the cost of RATs is less than that of the PCR tests, the overall cost can be considerable if used indiscriminately. The reported sensitivity of detection concerns for RATs means that consideration must be given to the probability of incorrect results and the potential impact for the individual and public health. These tests have a role when in a program of repeated testing likely to identify individuals when viral loads are high.

Antibody Testing

Antibody tests do not identify the virus, rather they indicate that the body has mounted an immune response to the virus. These antibodies appear in circulation one to two weeks after infection. They can therefore indicate that an individual has been exposed to the virus, either via infection or through vaccination. Given that it is unclear how long immunity remains post infection or vaccination it is possible that antibody testing may be used to assist decisions on booster vaccination.

Detection of Variants of SARS-CoV-2

Viruses mutate. Mutations occur when the virus is replicating in a host. The more the virus is

replicating the greater the chance of mutations. Mutations that have a competitive advantage will flourish and eventually become dominant. There have been waves of infection from different variants over the past year, specifically the alpha and delta variants. Each of these variants has been more infectious than the previous one.

As infection cycles wane and a new variant is becoming dominant it is important that this change is identified quickly, and appropriate measures put in place. This can only be done if detected cases are subject to whole genome sequencing. The WHO and European Centre for Disease Prevention and Control (ECDC) have a joint paper addressing the requirement for monitoring of variants.[7] They note that several variants of SARS-CoV-2 have emerged which are of concern. Emerging variants are classified as either Variants of Interest (VOI) or Variants of Concern (VOC). Monitoring of VOC in all countries is key. This requires sequencing of the viral genome. The cost and expertise required for this sequencing makes it impracticable for routine application.

Using alternative solutions such as the use of variation in response to multiple targets in PCR assays can triage those samples to be subjected to nucleic acid sequencing. In addition to identifying new variants by sequencing the impact of the variant must also be established; viral infectivity, its associated morbidity and mortality and the efficacy of vaccines. The impact of the variant on vaccine efficacy can be established using methods such as neutralization assays. The assays for sequencing and neutralisation require more sophisticated equipment and bio containment facilities that may not be available in routine clinical diagnostic laboratories.

COVID: The European Dimension

The impact of and response to COVID in Europe has not been uniform. Initially the infection presented in Italy with devastating loss of life. As the tragedy unfolded other countries had time to build defences. The healthcare authorities put triage systems in place and worked to ensure the hospitals were not overrun. The virus is primarily a respiratory virus, but it was some time before it became clear that the main route of transmission was aerosolized droplets.

Clinical diagnostic laboratories in Europe are configured in different ways with different funding models. These variations meant that the capacity to respond for the required testing varied. The scientists in China worked collaboratively with their global colleagues and the genomic sequence of the virus was published permitting preparation of primers for molecular assays. The IVD industry worked with remarkable speed to prepare testing kits for use on existing platforms. Virology laboratories, with research capacity, quickly developed 'in house' methods for testing.

The early period of the pandemic was characterized by a shortage of reagents for testing. In some cases, this led to a rationing of testing and conservation of supplies. Countries with large laboratories and large budgets were able to use their purchasing power. Differing testing protocols were used with some countries instituting mass testing in dedicated laboratories and others using distributed testing throughout their existing clinical diagnostic laboratory network. Many countries did not have the required testing capacity and there was cooperation between countries with many availing of capacity available in Germany. Specimen transport was facilitated by air forces.

European Country Responses

Members of the European Association for Professionals in Biomedical Science (EPBS) have recorded their national responses highlighting the essential role of biomedical scientists in the response.

Croatia

In Croatia, the fight against the COVID-19 pandemic is like that in most European Union (EU) countries. The government, Ministry of Health and the Civil Protection Headquarter issue recommendations and directives on measures to combat the pandemic. PCR tests are performed in most hospitals and the Institutes of Public Health, while antigen tests are performed in primary health care centres. The central hospital for the care of the most difficult patients as well as for the sequencing and coordination of laboratories that perform

PCR tests is the Clinic for Infectious Diseases in Zagreb.

Biomedical scientists at all levels have, as before, borne the greatest burden in laboratories for testing on SARS-CoV-2 because their knowledge, skills and competencies could contribute to the diagnosis of COVID-19. The status of Master of Biomedical Science has unfortunately not changed. Although in this pandemic, they have proven to be a valuable part of the team of healthcare workers. It is hopeful that the Government and the Ministry of Health will correct this injustice and that those with Master of Biomedical Science will improve in status like in most countries of Europe.

Iceland

In Iceland, the first quarantine orders were given in February 2020. The first COVID-19 domestic infection was confirmed in March 2020 and the first restrictions followed. From the beginning of the pandemic the screening and analysing of the Covid samples was manage by the heads of the Clinical Microbiology department at the University Hospital Landspítali (SVEID) who are a Biomedical Scientist and Doctor both specialists in Infectious Diseases. They had the technology, isolation and PCR equipment needed to analyse COVID. When Icelandic authorities decided to start screening, on a large scale, for COVID at the border as well as in the community, assistance was received from a private company with access to their facilities, equipment and, in the beginning, some professionals. Capacity at SVEID was insufficient in the beginning but it changed when they received improved facilities and new research equipment in late 2020. With new analysers productivity multiplied. The laboratory could not fill all the positions needed with Biomedical Scientists, so they also hired biologists, other scientists, engineers and students from scientific fields to work screening-related jobs for Covid-19.

Only two official and one private laboratory do Covid PCR tests and serum antigen tests. A few private laboratories do rapid antigen test which are all on the “Common list of rapid antigen tests” and one of them does serum antigen test as well.

There has been a shortage of Biomedical Scientists in Iceland for many years as in other European countries. Biomedical Scientists are a highly competent profession. Our work is interesting, diverse, demanding, joyful and requires specialized knowledge. According to Icelandic law from 2006 Biomedical Scientists in Iceland are authorized to own, run and manage laboratories. According to our operating license we have the authority to perform, interpret, validate, and approve results. But it is always doctors that diagnoses people. All information on COVID-19 available on covid.is

Ireland

Using Ireland as an example the response of laboratories was one of collaboration rather than competition. Initial testing was performed by the National Virus Reference Laboratory using an ‘in house’ method developed using internationally supplied primers. The biomedical scientists managing the laboratories came together, meeting weekly and, with the assistance of management consultants and the health service executive, identified the testing platforms needed for a hub and spoke model of testing. The platforms chosen depended on the size of laboratory and the testing catchment area. Following failure to deliver agreed testing kits by some companies, there was diversification of methods across the country with each hub laboratory having access to both batch analysis and rapid molecular testing. As the capacity was being commissioned, the samples from mass testing of the population were outsourced to Germany. Such was the dedication and commitment of the biomedical scientists to this project, that individuals drove across the country to ensure colleagues had the reagent supplies they needed. The scientists from research institutions, universities and veterinary testing laboratories were harnessed into the testing program. Each different group brought their own expertise from molecular testing of researchers to the clinical laboratory organization and sample tracking of biomedical scientists. The response to this virus highlighted the shortage of qualified biomedical scientists in Ireland.

Malta

In Malta, preparations for the anticipated

increased demand for laboratory services linked to the local spread of SARS-CoV-2 infections started early. The suspension of specific, non-urgent health services led to a decrease in workload which was usually received in various pathology sections. This allowed management to increase the staff working within the molecular diagnostics lab responsible for all COVID testing. Staff working in other sections were retrained and deployed to this section to increase human resources. New staff was also recruited and assigned duties related to COVID testing. Biomedical scientists working within university were also employed to ensure that every possible resource was being used. Additionally, our biomedical scientists were involved in managing and giving trainings to non-laboratory healthcare workers and moreover performing spot-checks in these remote clinics, hospitals and hubs involved with Covid-19 rapid testing. All of this has helped to keep up with the ever-increasing demand for COVID tests. Different rosters and teleworking were introduced to mitigate against any outbreaks within biomedical scientists. This was very important since laboratories located within the main public hospital are the main medical diagnostic facility and need to cater to the needs of the entire country.

Netherlands

In the Netherlands, a national network was set up in 2008 to deal with outbreaks of new infectious diseases in a coordinated way with laboratories being coordinated by the National Institute for Public Health and the Environment (RIVM). At the start of the pandemic a rapid and high-quality roll-out of the necessary diagnostic capacity and expertise were facilitated. The scaling up (rolling out of diagnostics) takes place in various phases, with the degree of scaling up depending on the expected course of an outbreak. Currently, 81 laboratories are accredited (ISO 17025 or ISO 15187 or ISO 22780) to perform molecular diagnostic tests for SARS-CoV-2. Initially, during a period of huge demand for testing, the samples were outsourced to Belgium and Germany. Biomedical scientists contribute greatly in processing laboratory results for SARS-CoV-2, they perform analyses, validate and interpret results and are responsible training of non-laboratory or less educated laboratory personnel when there are shortages. The knowledge, skills and competencies of the biomedical scientist is indispensable within the multidisciplinary team.

Portugal

In Portugal, the SARS-CoV-2 testing situation was like the rest of Europe. The government issued special directives regarding where and when massive testing could be performed, and by whom. The Instituto Nacional de Saúde Doutor Ricardo Jorge (INSA), jointly with Health Minister and Direção-Geral de Saúde, coordinated the Portuguese answer to this pandemic. The INSA is the authority responsible for accreditation of laboratories to perform SARS-CoV-2 NAAT. Portuguese bio-medical scientists were included in these directives, recognizing their knowledge skills and competencies in this area. Regulation of this activity is fundamental, to have the right professionals acting at the different stages of analysis is crucial. Therefore, Portuguese authorities allowed biomedical scientists to act as laboratories directors, performing, inter-preting, validating and issuing results under specific conditions. This is seen in Portugal with the massive testing program run by Higher Education Institutes in collaboration with the Portuguese Red Cross.

Sweden

In Sweden, from the beginning of the pandemic outbreak the public health agency was given the authority to provide recommendations related to restrictions and testing strategies. They were also responsible for the support to the diagnostic laboratories to maintain testing assays with high performance levels. All regions in the country were following the recommendations without exceptions. As everybody knows, the restrictions in Sweden differed very much from other countries in Europe resulting in almost no lockdowns. In the beginning, the testing strategies mainly focused on the hospitalised patients but with the escalation of the pandemic the testing strategies changed very quickly to be very generous. The laboratories in Sweden were unfortunately not prepared for this quick change that forced the laboratories to prepare

for a 1000-fold increase in testing in less than one week. Fortunately, some mass testing laboratories were prepared to receive many of these samples. Within the regions, the strategy changed so that tests from primary care patients were sent to the mass testing laboratories.

In the beginning, the testing of SARS-CoV-2 was dominated by PCR-tests performed in clinical laboratories mainly by biomedical laboratory scientists (BLS) but the lack of BLS in the bigger university hospitals forced the management to use other less educated individuals but, in their opinion, still educated enough to perform the tests. Later, a large-scale implementation of rapid diagnostics for SARS-CoV-2 antigen happened again in a short time. As the tests were new and the users in many cases had limited knowledge of the type of analysis, there was a need to ensure the quality of the entire chain at the national level; from choosing a quick test supplier to handling the sampling. Equalis (EQA provider) offered to perform an external quality assurance program during this time. The results were very clear, tests performed outside the clinical laboratories had less accuracy than the same tests performed by BLS despite very good implementation programs. These results were reported nationally, once again confirming the importance of BLS in health. The results are soon going to be published in an international journal.

Europe learned from the response to testing and instituted a more coordinated approach to the purchase and supply of vaccines. This ensured that all countries within Europe have access to the vaccines and no one has been left behind. As waves of the virus pass through populations and mutations occur the concept of zero COVID is no longer a possibility, and we must all learn how to live with this virus.

European Union (EU) Regulation and the EU Digital COVID Certificate (EUDCC)

Within the EU Healthcare is a national competence and each country makes its own decisions on how it will be configured and delivered within each state. An exception to this freedom within the EU is the directive governing the free movement of professionals. This system ensures that regulated professionals in one-member state may seek to practice the profession in another. This directive balances the entitlement for free movement to address the health and safety of the public. Similarly, the threat of this pandemic requires wide response across Europe.

Part of this response, in keeping with the CE marking of testing systems, is regulating the use of rapid antigen tests for COVID-19. The Health Security Committee (HSC), with expert representatives from each member state, decides on which rapid antigen tests (RAT) should be accepted. This list is updated regularly.[8]

The COVID-19 pandemic has had a huge impact on international travel, including in Europe and at the EU level. As part of the EU strategy to re-establish free movement the EU Digital COVID Certificate (EUDCC) was developed and implemented. The purpose of these digital certificates is to show that an individual can travel and cross borders without a (tangible) risk of carrying the virus. The EUDCC comes in three forms. Especially when it comes to the test and recovery certificates the professional expertise of the registered biomedical scientist becomes clear. For epidemiological safety it is crucial that tests such as PCR and other NAAT are performed in the correct way.

EU Digital COVID Certificate

The EUDCC comes in three forms:

- **Vaccination Certificate.** Confirmation that the holder has completed vaccination.
- **Test Certificate.** Confirmation that the holder has tested Negative for COVID-19; NAAT or RAT.
- **Recovery Certificate.** Confirmation that the holder was previously confirmed infected by SARS-CoV-2 and that this infection was identified by a 'Detected' or Positive COVID-19 NAAT.

According to EU Regulation on EUDCC, all testing used for the certificate, NAAT test or RAT test must be carried out by a health professional or by skilled testing personnel in

the member state issuing the certificate. It is important that tests are performed in the correct manner according to regulation and professional ethical guidelines. All such testing must be subject to quality assurance, ideally in centres accredited as ISO 15189 or 17025. For the safety of the citizens of the EU it is imperative that all testing processes are quality assured. Without this assurance the EU Digital COVID Certificate cannot succeed, and free movement will be curtailed. It is the position of EPBS that only regulated healthcare professionals, ideally biomedical scientists, should carry out such testing for the issuing of these certificates.

European Centre for Disease Prevention and Control (ECDC) is supporting scaling up of sequencing and neutralization assay capacity in EU/EEA Member States.[7] This development is both welcome and vital for the coordinated European response to this pandemic. It will also require investment in the education and training of additional biomedical scientists in Europe to be sustainable.

While we were ill prepared to respond to this current pandemic the citizens of Europe will not look kindly on their politicians if they fail to invest now to ensure we can respond to future threats. The investment in genomic capacity and expertise will also bring dividends in characterization of cancer tumors and other genetic conditions, in addition to supporting prenatal diagnosis of genetic defects.

The Biomedical Scientist and COVID-19

Biomedical scientists are a hidden profession within healthcare. Their work is critical to diagnosis and monitoring of all diseases. They are a profession of highly skilled scientists, educated in the biological basis of disease and the analytical method for ensuring safe and consistent analysis of biological specimens. The range of analysis covers clinical biochemistry, hematology, histopathology, immunology, microbiology, transfusion and transplantation sciences and virology. Their services are provided in clinical diagnostic laboratories 24/7/365 days. The analytical methods range from microscopic observation through chemical and immunoassay to use of molecular diagnostics. Within healthcare the work of clinical diagnostic laboratories is subject to rigorous monitoring with most laboatories operating to the ISO 15189 standard.

While much has been written about the healthcare staff on the front line during this pandemic, those in patient facing roles, the contribution of biomedical scientists to the control of this pandemic must not be underestimated. For a virus almost unknown in 2019 there have been almost 3 billion tests carried out within 18 months. This testing has been carried out in addition to the routine clinical diagnostic laboratory workload required for population health.

In addition to the analysis of samples, the biomedical scientists have worked with clinical colleagues to ensure that the correct specimens are submitted for analysis, and that the microbiologists and infectious disease teams are provided with analytical results and surveillance data. They have interacted with public health teams. They have provided the statistical data necessary for health providers and governments to manage the pandemic and make informed decisions.

In our introduction we highlighted the lack of preparedness of the world and the healthcare systems to respond to the COVID-19 pandemic. This was particularly true in terms of clinical diagnostic capacity. Over the past decades there has been an assumption that this specialty is becoming simplified with the introduction of automated analysers and integrated IT systems. There has been a trend to use non-professionally qualified staff and to reduce investment in the professional development and career pathways for biomedical scientists. This has been a mistake. As the pandemic unfolded it was evident that there were insufficient qualified biomedical scientists in Europe to undertake the range and volume of testing required. We need to prioritise the investment of the education and training of this profession now to ensure we can emerge from this pandemic and prepare for the next one.

The development and delivery of vaccination has been a game changer in the fight against this virus, however, the war is not yet won. The

work of the biomedical scientist is not yet over. As we look to the future for a successful emergence from the cycles of this pandemic, we will need a European wide system for virus identification that quickly identifies emerging infections, either via virus mutation or breakthrough infections. We need a responsive sequencing capacity to identify and monitor emerging variants tracking them from interest through concern. In addition, we need ready access to monitoring of immune response to inform the program of vaccine boosters.

The legacy of this viral infection will be a challenge. Already we see many presenting with 'long COVID' and hear talk of 'brain fog'. In pregnant women we have seen cases of devastating stillbirth from COVID placentitis. The long-term monitoring of the sequelae of this infection will require the knowledge skills and competence of biomedical scientists. Of concern is the demonstrable loss of cognitive function following this infection. We must do all in our power to ensure that this is not a legacy we leave to future generations and thus the testing and monitoring of infection in children must be given more attention.

The biomedical scientists of Europe, represented by EPBS, are your Diagnostic Partners in this fight. We will continue to work for the health benefit of our countries and together we can harness a resource that is at the disposal of the EU. Work with us, take advantage of our knowledge skills and competencies, give us the tools we need to deliver the service required, bring us into the discussion and, as we have demonstrated, we will deliver.

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