Enzo Biochem, Inc.

COVID-19 Related Challenges in the U.S. Diagnostic Sector and Enzo's Distinctive Response

March 2021

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03-01-2021

Abstract

While the U.S. and global response to the spread of SARS-CoV-2, the causative agent of COVID-19, is far from over, there is broad and continuing evidence that healthcare systems (including leaders in molecular diagnostics) were unprepared to address the health challenges associated with a pandemic of this scope and duration. Diagnostics companies and the network of laboratories positioned to provide testing services faced challenges including access to testing supplies, coordination of testing services, and the ability to scale up to meet demand as the number of infections rose. This paper presents an overview of the diagnostics sector highlighting structural inadequacies that negatively affected the ability of the U.S. healthcare system to respond to the COVID-19 pandemic. The document also includes an outline of best practices that can improve the ability to respond to future regional or global health crises. This response requires a rapid and sustained call to action from the diagnostics sector, including an assessment of the most effective molecular testing strategies and other related laboratory products and services.

As of February 2021, the U.S. had more than 28 million confirmed cases of individuals infected with COVID-19, and more than 500,000 deaths (~ 1.8% mortality rate). From the onset, the rapid spread of COVID-19 has placed unprecedented strains on all areas of our healthcare system, including a high demand for effective and readily available diagnostic molecular testing products and services. In a pandemic associated with an infectious agent such as SARS-CoV-2, broad access to accurate and rapid diagnostic testing is a central component in efforts to assess incidence, rates of infection, and optimal strategies in risk reduction and patient care. Failure to meet testing requirements early in the COVID-19 pandemic highlighted many shortcomings in the diagnostics sector, including lack of coordination of testing services, limited testing capacity, and inefficiencies in the production and distribution of reagents and other testing supplies. These challenges highlight several fundamental flaws in both the structure and operation of the clinical diagnostics industry in the U.S.

Case Study: Industry Response to COVID-19 Pandemic

Enzo Biochem is a life sciences and biotechnology company with three wholly owned subsidiaries:

- **Enzo Life Sciences**, focused on research and development, manufacturing, and marketing of biomedical research products and tools;
- **Enzo Therapeutics**, developer of therapeutic products; and,
- **Enzo Clinical Labs**, CAP accredited, NY Health Department and CLIA certified operator of regional clinical laboratories.

The company structure is unique in the diagnostics sector, bringing together the full range of resources necessary to develop new molecular testing modalities. Within this structure, Enzo is able to respond to demands for diagnostic testing technologies and services, from development through regulatory approval, and all phases of manufacturing and distribution including central lab facilities able to process samples.

This structure also positions Enzo to support third parties in development and delivery of testing services in business models that do not possess capabilities in any phase of the testing continuum, from development of new testing platforms to processing and reporting testing results. Following is an outline of strategies rapidly implemented at Enzo Biochem in response to COVID-19. The response positioned the company to consistently meet demand for testing services while addressing the challenges inherent in established standards in development and implementation of testing technologies in response to the pandemic. The results of the company's strategic response to COVID-19 highlight several opportunities to improve the design and delivery of diagnostic testing services in the U.S. and around the world.

Enzo response to COVID-19 highlights the need for testing solutions that are flexible and adaptable to most workflows, from sample collection through RNA extraction and nucleic acid detection. Strategies also require rapid and uninterrupted sourcing of required materials designed to minimize supply chain constraints. This strategic plan was designed to address the significant challenges associated with the widespread use of closed testing systems in the diagnostics sector.

As a first stage in the response to COVID-19, Enzo worked to developed new molecular tests and position them for Emergency Use Authorization from the FDA. For immunoassay development, Enzo targeted the appropriate markers (SARS-CoV-2 receptor-binding domain [RBD] of the spike protein) for antibody detection to accurately assess past COVID-19 exposure and infection. These assays may also aid in the detection of the most recent SARS-CoV-2 variants because the most prominent variants have mutations in the spike (S) protein gene [1]. Enzo's molecular tests targets the nucleocapsid (N) protein gene. Computational comparisons between these most prominent SARS-CoV-2 variants revealed that Enzo's molecular probes are not impacted, making Enzo's molecular test capable of detecting currently circulating variants and sub-variants.

Enzo's diagnostics tests include two methodologies: RT-qPCR technology (**molecular/swab test**, Figure 2) that detects the presence of the virus via nucleic acid analyses, primarily during an active infection, and immunoassay technology (**serological/antibody test**, Figure 3) that detects antibodies produced in response to coronavirus infection and, potentially, neutralizing antibodies (NAb) post-immunization (e.g. vaccination). As a tie-in to development of new testing technologies, Enzo also took steps to address challenges in patient access to testing services, and issue that has significantly hindered the ability to generate accurate data about incidence throughout the pandemic. In November 2020 the company launched an online platform that enables patients to schedule a test without having to first visit a doctor's office, which was positioned as a significant barrier to access for many patients. The service includes an electronic rapid physician-authorization for molecular and serological laboratory testing accessible at laboratory locations near consumers.

- The Enzo's swab test (AMPIPROBE® SARS-CoV-2) is a highly sensitive EUA assay that aids in the detection of SARS-CoV-2 infection (Section 1).

- A negative Enzo swab test accompanied with a positive antibody test (SARS-CoV-2 IgG ELISA) suggest that the person is less likely to have an active viral infection and is no longer capable of transmitting the virus (Section 1 and 2).

- A positive Enzo IgG antibody test indicates that a person has mounted an immune response to the SARS-CoV-2 viral antigens, either from natural infection or as a result of vaccination.

- Enzo's IgG antibody test correlates with the presence of a neutralizing antibodies, suggesting an effective immune response (Section 2.2).

- In November 2020 the company launched GoTestMeNow.com, an online platform that enables patients to schedule a test without having to first visit a doctor's office.

- Ongoing epidemiological surveillance testing together with strategies in social distancing, use of masks and disinfectants remain the best strategy against COVID-19.

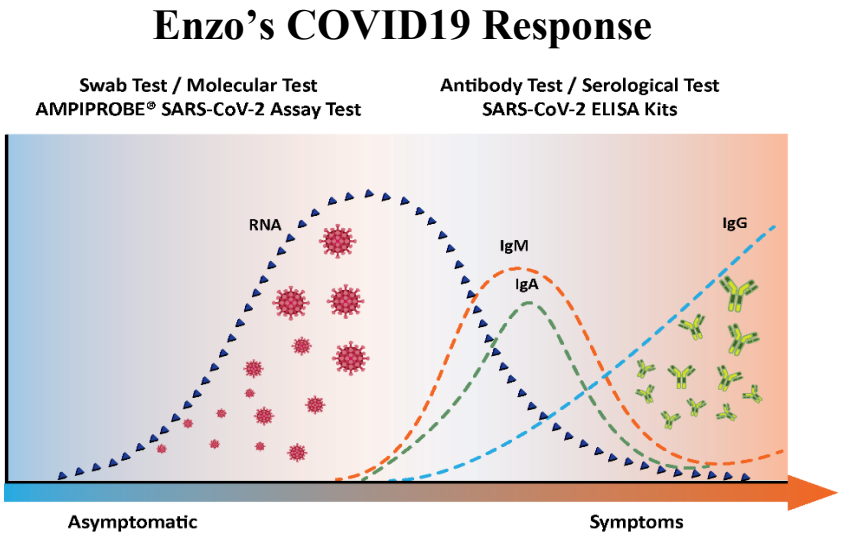


Figure 1. Enzo's diagnostic tools against the COVID-19 pandemic: The swab test identifies SARS-CoV-2 particles during active infections, while the antibody test measures patient's response to resolved past infections.

Enzo's Molecular Solutions Using RT-PCR

Enzo's AMPIPROBE® SARS-CoV-2 Test System under the FDA's Emergency Use Authorization (EUA) includes proprietary AMPIPROBE® technology, buffer solutions, Taq polymerase, and SARS-CoV-2 specific primers; thereby providing a cost-effective, high-performance (Table 1), and adaptable solution for the clinical diagnostics market.

Enzo's EUA approved AMPIPROBE® SARS-CoV-2 Test System is a complete workflow solution designed for the molecular detection of SARS-CoV-2 virus that includes:

- AMPICOLLECT™ for sample collection*****
- AMPIXTRACT™ SARS-CoV-2 Extraction Kit for sample processing - nucleic acid extraction from patient specimens
- AMPIPROBE® SARS-CoV-2 Assay Kit and Controls for amplification and detection

***** *Note: AMPICOLLECT sample collection is not required by the FDA but is manufactured by Enzo to offer a complete integrated solution with EUA authorized products. It is equivalent to sample collection offered by competing brands.*

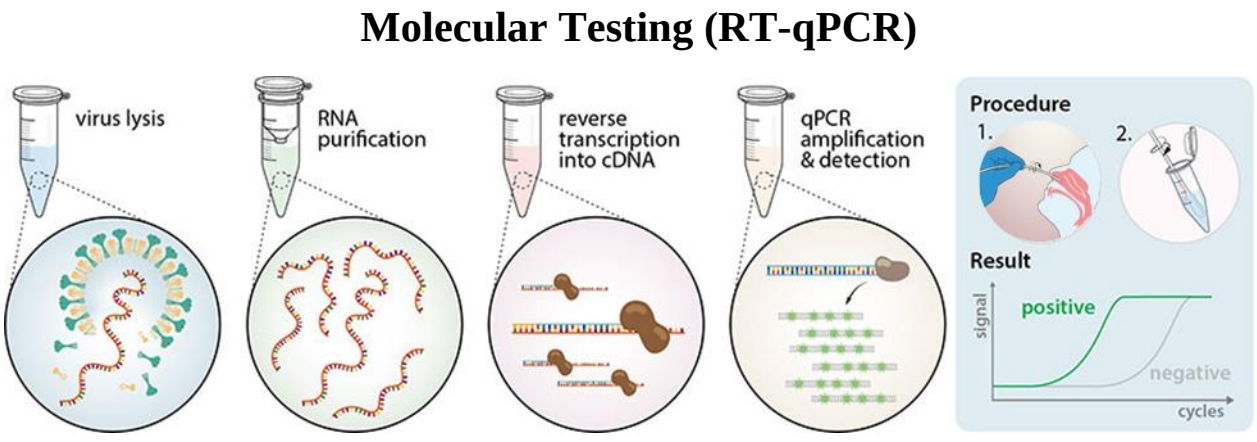


Figure 2. Basic Principle of Nucleic Acid Amplification Test (NAAT) COVID-19 Test. Viral RNA is harvested and purified, followed by transcription into cDNA and subsequent amplification and detection by quantitative PCR.

The AMPIPROBE® SARS-CoV-2 Test System allows for the molecular detection of SARS-CoV-2 viral RNA using the GENFLEX™ platform, an open, high-throughput, automated, and scalable platform to execute molecular diagnostic tests within a clinical production setting. The system provides a flexible and fully automated platform that consists of a pipetting module for sample extraction and PCR set-up, and a qPCR module for nucleic acid amplification, detection, and data analysis.

Clinical Performance of AMPIPROBE® SARS-CoV-2 Test

		Reference Test			
		Positive Patient Specimen	Inconclusive Patient Specimen	Negative Patient Specimen	Total
AMPIPROBE® SARS-CoV-2 Test System	Positive Patient Specimen	**51**	**0**	**0**	**51**
	Inconclusive†	**1**	**0**	**3**	**4**
	Negative Patient Specimen	**1**	**0**	**144**	**145**
	Total	**53**	**0**	**147**	

Table 1. Clinical performance of the AMPIPROBE® SARS-CoV-2 Test System in nasopharyngeal swab specimens

The positive and negative percent agreements between the AMPIPROBE® SARS-CoV-2 Test System and FDA EUA tests are:

Positive Percent Agreement = 51/53= 96.2%, CI [87.3% - 99.0%]

Negative Percent Agreement = 144/147= 98.0%, CI [94.2% - 99.3%]

Inconclusive Rate = 4/200 = 2.0%

†Note: There was insufficient material to re-test samples with inconclusive results.

Serological Testing

While molecular (RT-PCR) tests serve as the frontline diagnostic tool to combat the COVID-19 pandemic, serological tests can be used to detect antibodies produced by a patient's immune system in response to infection by the SARS-CoV-2 virus [2]. Antibodies continue to be present after recovery from COVID-19, making it possible for serological tests to be used to confirm past infection. Importantly, serological tests also have the potential to be used to assess the degree to which a patient has produced antibodies following a vaccination, anticipated to be an important measure of patient outcome. Although the CDC has offered guidance for the use of serological testing in clinical settings, the level and duration of immunity provided by circulating antibodies in recovered or immunized patients remains unknown. Researchers anticipate that serological testing will provide important insights related to infection rates, seroconversion timelines, levels of acquired immunity through vaccinations, and future epidemiological assessments of the COVID-19 pandemic.

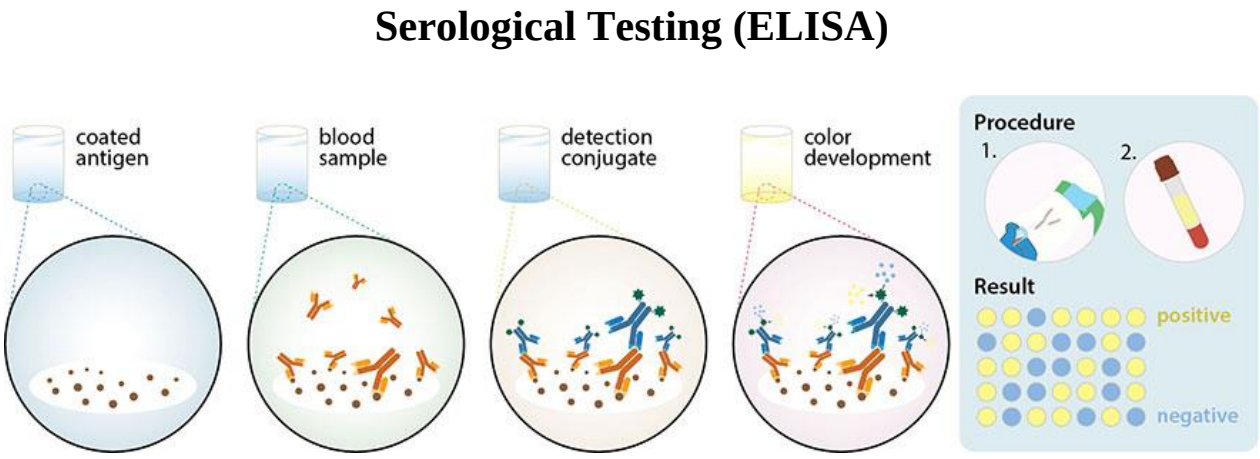


Figure 3: Basic Principle of Enzyme-Linked Immunosorbent Assay (ELISA) Serological Tests. Antigen-coated microplates are used and a blood sample, most frequently plasma, is applied. The anti-SARS-CoV-2 antibodies contained in the blood sample will be immobilized by binding to the coated antigen. A detection conjugate, an enzyme-coupled secondary antibody, binds to the immobilized antibody and catalyzes a chromogenic reaction.

Antibodies, or immunoglobulins, exist as several classes. Immunoglobulin M (IgM) is released as a pentameric antibody and is generally among the first responses of the humoral immune system [3]. IgA is primarily secreted as a dimeric antibody and plays a major role in the defense of the mucosal epithelia of the respiratory airways and intestines [4]. IgG typically appears later than IgM and forms the major component of the immune memory response and immunity [5]. For COVID-19 patients, seroconversion

appears to occur within several days after symptomatic onset, and serum antibody levels peak after 2-3 weeks. Although the canonical view of antibody production states a clear succession from IgM followed by IgG and then IgA, SARS-CoV-2 appears to induce an early and transient expression of IgA concomitant with IgM, followed by more durable IgG expression (Figure 6) [6]. How long IgG antibodies remain detectable following infection is currently unknown and an active area of investigation [7].

The efficacy with which the adaptive immune system develops an antibody response and establishes lasting immunity following SARS-CoV-2 infection is also currently under investigation. Studies using samples from hospitalized patients suggest that nearly all immune-competent individuals will develop an immune response against SARS-CoV-2 [8]. These results raise hope that lasting immunity can be achieved, as the genetic drift of SARS-CoV-2 has been shown to be substantially slower than initially feared. Additionally, crucial antigenic sites, such as the receptor binding domain (RBD) of the spike protein, seem to be relatively conserved. However, preliminary studies testing the general population indicate that minimal exposure to the virus or short disease courses with mild or no symptoms might not be sufficient to elicit a robust immune response [9]. Additionally, many preliminary antibody screening studies have been hampered by the type and quality of the serological tests employed.

Seroconversion Post SARS-CoV-2 Infection

To complement the molecular diagnostic AMPIPROBE® SARS-CoV-2 Assay, Enzo developed a SARS-CoV-2 IgG ELISA Kit. Enzyme-linked immunosorbent assays (ELISAs). ELISAs are used to detect the presence of proteins (e.g. antibodies) providing a semi-quantitative signal used for diagnostics. While the serological test is currently used in Enzo's clinical laboratories, it has been submitted for FDA Emergency Use Authorization (EUA). Enzo's molecular test (RT-qPCR) is currently authorized for emergency use. Enzo's ELISA assay is a qualitative assay optimized to provide accurate and sensitive detection of IgG antibodies to SARS-CoV-2 in human serum (Tables 2 and 3), with high-throughput testing capabilities for the clinical laboratory setting.

Performance of SARS-CoV-2 IgG ELISA Kit

		RT-PCR	
		Positive	Negative
IgG ELISA	Positive	**36**	**4**
	Negative	**0**	**109**

Table 2: Comparison of the SARS-CoV-2 IgG ELISA Kit results to the diagnosis based on the AMPIPROBE® SARS-CoV-2 RT-PCR Assay Kit as a reference.

Specificity = 96.5% Sensitivity = 100%

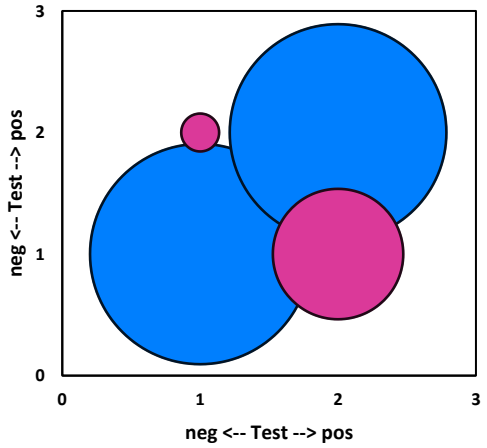
Reproducibility of SARS-CoV-2 IgG ELISA Kit

Control	Mean OD	SD	%CV	n
High Positive Control	0.77	0.08	10	15
Low Positive Control	0.166	0.006	3	15
Negative Control	0.068	0.002	3	15

Table 3: Intra-assay (within the same experiment) reproducibility expressed in terms of OD on 15 replicates of each provided controls.

The Enzo ELISA kits are qualitative immunoglobulin assays for the detection of IgG (completed; see Table 4 for *in vitro* comparison to other available kits, Figure 4 for comparison of reference clinical samples), IgM (in-development) and IgA (in-development) specific antibodies. The timing of specific immunoglobulin production and seroconversion plays a pivotal role in clinical testing and interpretation. During the early stage of infection, IgA and IgM antibodies are produced. As the levels of IgA and IgM drop, IgG levels rise and remain detectable during late stage infection and through recovery. During this seroconversion, the levels and detection of specific immunoglobulins allow for the identification of early infection (IgA and IgM) transitioning to post infection (IgG). Due to the time sequence of antibody expression, parsing out the pattern of expression for a given patient can offer clues to time of infection leading to more accurate contact tracing endeavors. Actively surveilling seroconversion of patients allows further understanding of the progression of SARS-CoV-2 infection and disease resolution.

Comparison of SARS-CoV-2 IgG ELISA Kit Using Clinical Samples



	Negative Reference	Positive Reference	Total
Negative Test (Enzo)	31	11	42
Positive Test (Enzo)	1	30	31
Total	32	41	73

Figure 4 Comparison Enzo's antibody test against a competitor with clinical samples.
Clinical samples were analyzed with Enzo's antibody testing against reference samples. The results show 83.6% agreement (73.4 to 90.35%),

In vitro Comparison of SARS-CoV-2 IgG Tests

		Enzo		Competitor 1		Competitor 2	
	# of Replicate	**3**		**3**		**3**	
		Average	**SD**	**Average**	**SD**	**Average**	**SD**
	Sample Diluent (negative control)	0.025	0	0.174	0.003	0.0167	0.006
	Original Sample (positive control)	31.7625	1.7174	141.13	1.415	7.93	0.335
Serial dilutions	1:2	25.12	0.3260	137.37	2.173	3.70	0.101
	1:4	16.60	0.3016	92.87	0.838	1.53	0.062
	1:8	9.32	0.4065	49.49	0.712	0.62	0.025
	1:16	5.00	0.4347	24.44	0.255	0.31	0.006
	1:32	2.45	0.1528	11.95	0.087	0.15	0
	1:64	1.20	0.0315	5.84	0.010	0.08	0

Table 4: Comparisons of different immunoassay kits: Enzo SARS-CoV-2 IgG ELISA kit; and two test from competitors. The same pooled positive IgG sample was run on all kits following each manufacturer's instructions. Reported index values higher than 1 denote positive detection of SARS-CoV-2 (red), values lower than 1 denote failure to detect viral particles (colorless).

Serological Surveillance Post Vaccination and Immunization

Immunization via vaccination prior to an infection stimulates the humoral immune response in a manner similar to the stimulation caused by a pathogen during the course of an infection. Accordingly, the immunity acquired after the body has successfully cleared an infection caused by a pathogen is similar to the immunity acquired post-vaccination. The active targeting units that can decrease the biological activity of a viral pathogen in subsequent encounters are called neutralizing antibodies (NAbs). NAbs bind specific motifs on the pathogen (epitopes) to prevent their biological function, thereby preventing or ameliorating infection. The recently completed phase 3 clinical trials of vaccines against SARS-CoV-2 (NCT04470427 and NCT04368728) closely monitor the development of NAbs as one of their outcomes to assess effectiveness. The two first COVID-19 vaccines approved for emergency use are both mRNA vaccines encoding the gene for SARS-CoV-2 spike protein [10,11]. After vaccination, cells temporarily uptake and translate the mRNA to protein, ultimately leading to an immune response (antibody production).

Currently, the FDA has authorized the use of a serological test to detect NAbs from COVID-19 convalescent individuals. The test is designed to identify individuals with an adaptive immune response to the virus. In the diagnostic test, a patient's serological sample (potentially containing antibodies against SARS-CoV-2 viral particles) is first incubated with the spike protein fused to a detection probe. The mixture is then allowed to interact with the ACE2 receptor fixed on a detection matrix. The human ACE2 receptor is the target that the SARS-CoV-2 virus uses to infect cells. If the patient's sample contains NAbs, the antibodies prevent the interactions between the virus spike protein fusion and the ACE2 receptor. Consequently, a decrease in signal in this competition assay is scored as the presence of NAbs. Similarly, Enzo's flexible SARS-CoV-2 IgG ELISA methodology can be used to detect antibodies that prevent the interaction between the spike proteins and the ACE2 receptor. Enzo's ELISA kit employs viral spike protein immobilized on a detection matrix (microplate wells). When recombinant NAbs are incubated in the microplate wells containing the spike protein (before adding the ACE2 receptor fused to a reporter), the interactions between the ACE2 receptor and the viral spike protein are disrupted, showing a decrease in signal (Figure 5A). Similarly, when clinical samples are processed in this manner, there is a clear inverse relationship between the levels of anti-SARS-CoV-2 antibody present and the amount of ACE2 receptor that can interact with the bound spike protein (Figure 5B). High levels of anti-SARS-CoV-2 IgG are associated with decreased detection levels of ACE2 receptor.

Antibody Disruption of ACE2 and Viral Spike Protein Interaction

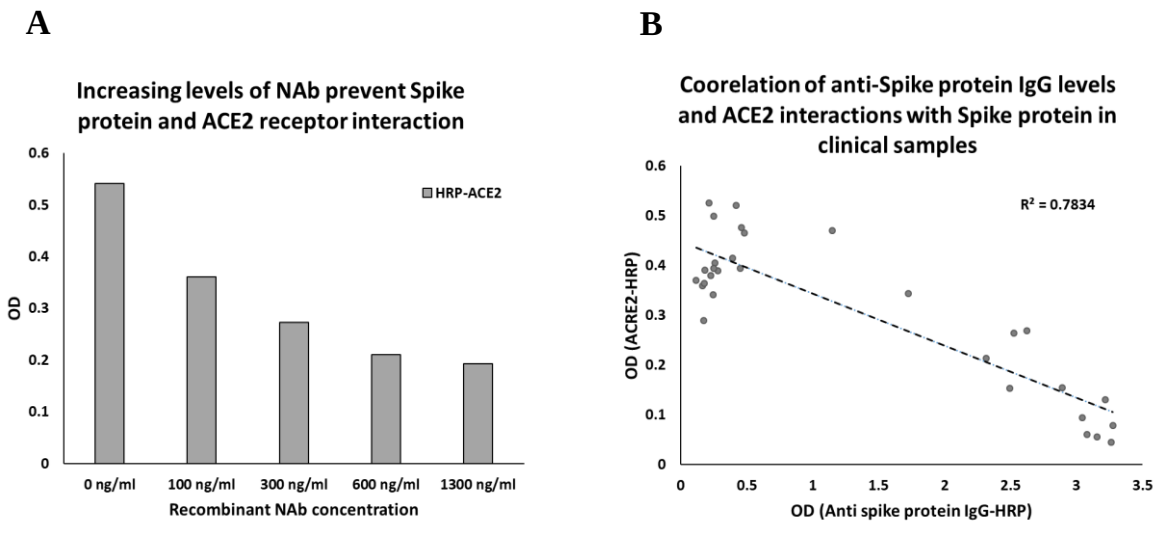


Figure 5: Anti SARS-CoV-2 immunoglobulins disrupt ACE2 interactions with viral spike protein. Enzo's Anti SARS-CoV-2 ELISA kit is used to assess the interactions between human ACE2 and SARS-CoV-2 spike protein. A) Increasing levels of commercially available recombinant NAbs destabilize ACE2 and Spike protein interactions (decreased signal at high Ab concentration). B) High anti SARS-CoV-2 IgG levels in clinical samples correlate negatively with the interactions between ACE2 and the spike protein.

Given the focus on NAbs expression in the adaptive immune response, Enzo researchers recognized the need for a reliable, sensitive, and accurate method to detect and quantify NAbs. Early results from clinical trials estimate the effectiveness of immunization due to vaccination to be over 90% [10,11]. In this light, it is relevant to develop methodologies for monitoring acquired immunity post-vaccination. To date, no approved methodology has been identified as a quantitative measurement to equate the presence and the level of antibodies in blood to levels of immunity against SARS-Cov-2. Within this framework, Enzo is advancing development of serological testing capabilities to address this continuing area of unmet need.

SARS-CoV-2 Humoral Response

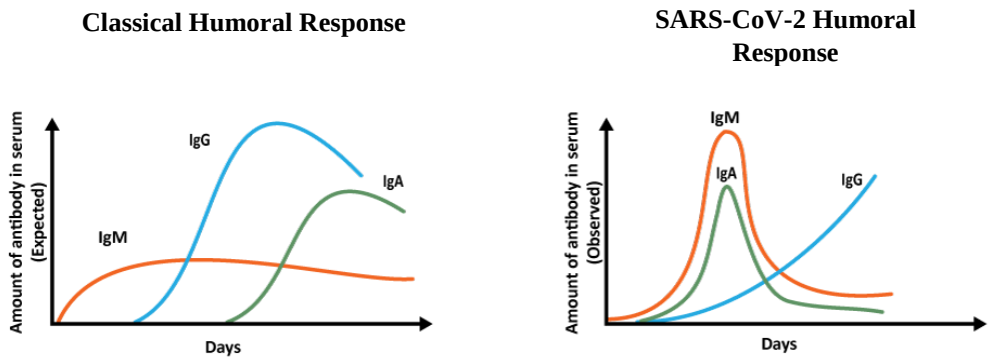


Figure 6: Comparison of canonical humoral response vs SARS-CoV-2 immunoglobulin expression pattern. Classical humoral response to antigen follows a sequential production of antibodies. First IgM are produced, followed by the predominant immunoglobulin IgG, and lastly IgA. Current investigations have indicated that SARS-CoV-2 elicits a different expression pattern, and early and transient expression of IgM and IgA, followed by IgG.

Limitations of Rapid Tests Such as Lateral Flow Tests

Rapid detection or point-of-care testing for serologic antibodies introduce their own sets of limitations. These tests, which utilize a relatively simple immunochromographic strip test (IST), are often called lateral flow tests (LFTs) and are similar in structure to common pregnancy tests. They rely on immobilized antibodies and colloidal gold-conjugated SARS-CoV-2 antigens for detection. Colloidal gold is composed of very small gold particles (5 - 100 nm) that appear intensely red when congregated. For serological testing, a few drops of blood, serum, or plasma are added onto a sample pad and passed over a detection stripe by capillary flow. On its way, the sample passes a conjugate/reagent pad, where it is mixed with the conjugated viral antigens. When a blood sample contains antibodies that bind the viral antigen-conjugate, an antigen-antibody complex is formed. The sample-conjugate mix passes further over the detection stripes, which are zones where anti-human IgG/IgM antibodies have been spotted. Here, the antibodies contained in the sample will be immobilized and, if they are bound to conjugated viral antigens, the detection stripe will be stained red.

Lateral Flow Test (LFT) Principles

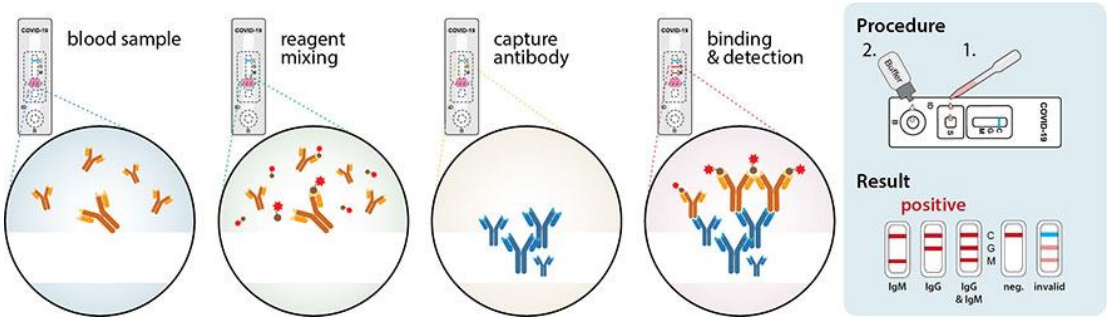


Figure 7: Basic Principle of Immunochromatic Strip Test (IST) Serological Tests. A blood sample is applied to the quick strip test. A buffer is applied to the reservoir and will distribute the sample through the test based on capillary forces. The sample passes a reagent reservoir, gets mixed with antigen-conjugate and IgM or IgG antibodies will be bound by capture antibodies in the detection stripe. If antigen-binding antibodies were present in the sample, the detection stripe will appear red.

LFTs are intrinsically hampered by the short incubation times defined by the capillary flow, the comparably small sample amounts, and the lack of wash steps, which limit the sensitivity and specificity of this assay type [12]. In April 2020, the World Health Organization (WHO) released a statement against LFTs highlighting issues with sensitivity varying from 34% to 80% [13]. Enzyme-linked immunosorbent assays (ELISAs) overcome this issue and generally offer significantly better specificity and sensitivity at the cost of requiring execution in a laboratory setting. Without any improvement in LFT technology, their lower specificity coupled with poor sensitivity can lead to a high rate of false negatives. Incorrectly diagnosing patients can increase the spread of the disease or instill a false sense of security regarding immunity and public safety. Additionally, due to the typical microplate format of ELISAs, these tests can be easily automated and allow high-throughput screening of hundreds of patient samples at one time. Enzo's position in the market and reliable access to key material supplies offer the possibility of extending serological test-based monitoring beyond past infection identification and prospectively into serological surveillance post-vaccination.

Direct Antigen Testing

In addition to standard RT-PCR molecular testing for SARS-CoV-2 acute infection, viral particles can also be directly detected by immunoassays. Direct antigen testing can be used to diagnose current infection similarly to viral RNA detection tests. Based on the same principle as ELISA detection of antibodies, viral particles can be detected directly during the acute phase of COVID-19. Antibodies against outer proteins of the viral particles (proteins accessible without lysing the virus) are placed on a microplate. Samples are then added to the antibody-coated microplate; if viral particles are present and bound to the antibodies, subsequent steps allow the detection and qualitative assessment of the amount of virus particles (viral titer).

Although direct detection of viral particles offers some advantages over RT-PCR molecular testing, it is limited by lower sensitivity and the requirement for high abundance of viral particles for reliable detection of the virus [12]. One feature of direct testing is the reduced time from sample collection to diagnosis versus molecular testing. Direct antigen testing as a point-of-care test can be performed at a doctor's office and within a short amount of time, leading to more rapid diagnosis and expediting the delivery of medical care.

Focus on Treatment

A positive SARS-CoV-2 diagnosis from a swab test (RT-qPCR) is inherently different than a positive antibody test (serological ELISA). A positive swab test indicates the presence of viral particles that are presumed to be virulent within the respiratory tract. With confirmation of infection, current guidelines recommend taking a series of steps to protect an infected individual as well as the general population, including closely monitoring symptoms, staying at home unless seeking medical care, and isolation. It is important to highlight that nearly 80% of individuals who test positive for SARS-Cov-2 infection will present no or only mild symptoms (e.g. fever, headache, nausea, and loss of smell). Around 15% of individuals will experience severe symptoms including difficulties breathing and need hospitalization and about 5% will experience critical symptoms that can require intensive care [14] and present a risk of death. At the time of symptom onset (~ 10 - 14 days post infection), viral load and particles have peaked and begin to decrease, while at the same time the humoral immune response (antibody production), mainly IgG, is ramping up. It is essential to understand the etiology of COVID-19 to efficiently and effectively treat the disease. The critical manifestation of COVID-19 is the result of an unregulated immune and inflammatory response. SARS-CoV-2 infection results in interstitial inflammation of the lower respiratory tract epithelium, endothelial dysfunction, coagulation complications, infiltration of inflammatory cells

into organs, and multi-organ failure [15]. Given the etiological nature of the symptoms, managing the dysregulated immune response (e.g. cytokine storm) and its associated complications could prove to be an effective treatment approach [16]. To that end, Enzo has submitted a patent application directed to the use of SK1-I, a small molecule inhibitor of sphingosine kinase 1, which has demonstrated a downregulation of inflammatory cytokines in animal models including interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-alpha), for the treatment of COVID-19.

A positive test detecting IgM or IgG can inform the patient of past SARS-CoV-2 infection. In light of the humoral response to the virus (Figure 6), distinguishing between the expression of IgM and IgG can provide a time window to the patient course of infection. High levels of IgM would indicate a recently resolved infection, while low levels of IgM and high levels of IgG would suggest a more distant infection. This information can inform vital follow-up steps for contact tracing and overall epidemiological investigations.

Conclusions

Challenges in the response to the COVID-19 pandemic from within the diagnostic sector significantly reinforce the need for both business structures and a regulatory climate that support the rapid introduction of reliable and cost-effective technology and service solutions. One example is Enzo's unique business structure that includes stablished capabilities as a developer, manufacturer, and clinical service provider, which positioned the company to plan and facilitate a quick response to testing needs and the ability to revise and expand access as necessary. For companies that do not have a similar structure, both innovation of products and service delivery within the sector should be positioned to help other players to expand their capabilities to keep pace with demand. One critical element in this strategy is the broader use of open-system platforms in diagnostic testing. Following are additional strategic recommendations based on analysis of industry response to COVID-19 in the first year of the pandemic:

- We must facilitate faster EUA reviews and approval, to deploy new technologies as quickly and efficiently as possible, as was seen with the deployment of the AMPIPROBE® SARS-CoV-2 Test System (swab/molecular test).

- We must have in place reliable serosurveillance that can be carried out at a central lab, as was evidenced with Enzo's SARS-CoV-2 IgG ELISA while pending EUA approval.

- The diagnostics sector must coordinate closely with leaders in digital technology to build on-line platforms such as GoTestMeNow.com to facilitate scheduling of COVID-19 testing with rapid electronic physician-authorizations.

- We must continue our focus on research that can position industry players to develop diagnostic technologies to address emerging threats more rapidly, and companies must invest in the infrastructure to support these research efforts with optimal efficiency.

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About Enzo

Enzo Biochem, Inc. (NYSE:ENZ) is a pioneer in molecular diagnostics, leading the convergence of clinical laboratories, life sciences and intellectual property through the development of unique diagnostic platform technologies that provide numerous advantages over previous standards. A global company, Enzo Biochem utilizes cross-functional teams to develop and deploy products, systems and services that meet the ever-changing and rapidly growing needs of health care today and into the future. Underpinning Enzo Biochem's products and technologies is a broad and deep intellectual property portfolio, with patent coverage across a number of key enabling technologies.

Enzo's Comprehensive COVID-19 Program is indicative of Enzo's ability to respond to the current challenges plaguing the healthcare market. The integrated company structure provides Enzo with an advantage of having direct access to patients while keeping control of the testing reagents and supply chain. Enzo utilizes its technological and research and development capabilities, manufacturing infrastructure strength, and clinical diagnostic knowledge to develop products that address gaps in performance, cost, obtainability and safety. Enzo is one of few companies to incorporate a biotech entity, diagnostics division, and a CLIA certified clinical laboratory within the same company. Enzo has addressed challenges of the supply chain by manufacturing all of its reagents in-house. Its diagnostics equipment and kits are proven in its own lab prior to being released for sale in the marketplace for other labs and end users.