COVID-19 and its Ripple Effect on Clinical Trials

Whilst pandemics are fortunately not common, the global impact of COVID-19 has been profound. At the time of writing, global deaths have reached 420,000 whilst over 7.5 million people have been infected. As optimism increases that the virus begins to be controlled and the impact to life is understood, some forecasts predict grimmer longer-term societal and financial consequences, across many countries. Whilst we should not overlook the tragic loss of life nor the impact to quality of life, there are positives we can take from this crisis.

This article will reflect on the impact on clinical trials, drug and diagnostic development. However, many parallels with daily life can also be considered. Growing through adversity is an oft used aphorism and one which is true of people and industries alike. When faced with challenges, human ingenuity knows no bounds and COVID-19 has been both the mother of innovation but also the catalyst for the broader adoption of existing technologies.

It is no surprise therefore that the clinical trial market has rapidly adjusted to the new paradigm, one defined by limitation of social interaction, by looking to leverage technological mitigations. Before we explore this statement further, it is necessary to also reinforce that clinical trials were far from perfect. This has long been understood and the financial imperatives of this inefficiency propelled the industry to reevaluate the approach. This has materialised over the last decade with a greater focus on the patient as the centre of the trial. Whilst a truism that a clinical trial is not possible without the patients, the view that research should be designed around the patients, often as individuals, is something which is now being routinely built into studies.

Clinical trial participation remains low, with the US leading the way, with 5.4% as of 2016 (Statista); however, outside of the UK, Germany, France, Spain and Italy, only South Korea has a rate greater than 2% globally. The reasons behind this are complex, often idiosyncratic or culturally defined, however broadly stem from the awareness, social/moral compulsions and the burden of participation. The latter point is key and bringing studies to patients, and not the other way around, will be the cornerstone of future research, one which brings together digital health technologies with point-of-care testing and advanced supply chains. With the world in need of heroes, frontline workers across the world stepped up, with many placing themselves in clear personal danger. At the same time, the situation offered a degree of redemption for the increasingly vilified pharmaceutical industry. For many working within the industry at large, their critical roles in developing new vaccines, therapeutics and diagnostics never had such prominence, urgency or clarity of need. We saw unprecedented collaboration between competitors, regulators and academia to help solve the crisis. These new partnerships have the potential to revolutionise the way that we develop medicine in future. The hope is that all of this leads to a greater focus and commitment to human health. Events of the last few months have only reinforced the fragility of our existence and a collective responsibility to help each other. We are still without any vaccine against the Sars-CoV-2 virus and should not anticipate broad access to one for a long time yet. Antiviral medication to ameliorate the impact of infection is also in development; however, with the hope of repurposing existing treatments this may be sooner to arrive. Like the global economy, clinical trials are facing major disruption as research professionals seek to overcome unfamiliar challenges. Processes taken for granted had to be speedily revisited. Governments across the globe have instigated the necessary measures to 'flatten the curve' and limit the number and rise of COVID-19 cases. Alongside limits due to constrained supply chains, regional limitations and even company restrictions, hundreds of clinical trials have been significantly affected with the global average standing at -79% reduction in patients entering studies year-on-year (Medidata COVID-19 Report v.5). Whilst anticipated, there is no assurance another pandemic will hit again, when that might be, or what the impact would be like. Taking the learnings from COVID-19, we know we can build on this opportunity to find innovative alternatives to set new standards that allow us to respond with flexibility and pragmatism. The industry has been historically slow to embrace new technology with EDC taking decades to become established. The adoption curve for digital and virtual trials will hopefully be greatly expedited by the pandemic.

Pre-COVID-19 vs Post-COVID-19 – Clinical Trial Challenges Revealed

Whilst the industry is focusing on developing vaccines and therapies in response to COVID-19, the crisis has significantly disrupted clinical trials in other therapy areas, most notably cardiovascular, dermatology and metabolic. Even though major regulatory agencies such as the FDA and EMEA have instigated guidelines and measures for maintaining the integrity of the trials, that seek to ensure the rights, safety and wellbeing of patients and healthcare staff during this COVID-19 pandemic, keeping clinical trials on track has been severely challenged. The COVID-19 pandemic has truly shaken up the world and the consequences on the conduct of clinical trials are many, including, but not limited to:

- Concerns about safety of the patient combined with the reallocation and hence lack of staff or resources to accommodate these patients have led to a decreased and/or delayed enrolment of patients
- New study initiations were put on hold by either the industry itself, or forced by regional lockdowns, which resulted in patients being prevented from entering trials and visiting hospitals
- Overwhelmed hospitals, resources, and systems
- Reprioritisation of new test applications to only those that treat, diagnose, or prevent COVID-19; clinics allowing only these essential or critical visits, and refusing to take part in trials

- Conversion of physical visits into virtual visits
- Extension of the duration of the trial, as the study was either interrupted or slowed down during recruitment
- Recruited patients having to drop out of the trial
- Vendors and contractors unable to meet obligations, such as delivering drugs to sites
- Disrupted supply chain due to closed borders, also impacting shipment of clinical trial samples to be tested by a central laboratory
- Risks of compromised data integrity if new procedures are deviating from the original plan

There is an obvious need to mitigate risks for patients and to support their inclusion into clinical studies. Flexibility, innovation and use of available technology will be of utmost importance to manage in this new paradigm. Beyond COVID-19, sponsors will be looking to dramatically accelerate patient recruitment and enrolment to catch up with lost time. Looking ahead, we believe the following challenges are pivotal for turning future clinical trials into a success:

- Have a clear view and understanding of the evolving situation
- Reconsider standard trial design and setup to enable data capture
- Be flexible and accelerate study start-up
- Above all, maintain quality and supply chain.

At Cerba Research, we understand the situation is highly dynamic and region-dependent. We have integrated solutions in place to address each of these abovementioned challenges; from providing insights into metrics and trends, to virtual and nimble solutions and centralised data. Even though a remote workforce and disparate operations have become the new norm, we have taken first steps back to normal operations, and are building beyond standard to remain resilient and agile.

Labs are Overwhelmed with Multitude of Assays for Identifying COVID-19

When it comes to the clinical trial space, we need to ensure inclusion/exclusion criteria are well defined as they set the framework for enrolment of patients. Given the current global prevalence, sponsors will need to consider routine inclusion of COVID-19 testing during screening in order to rule out positive patients in the course of the trial. Since the emergence of the pandemic, numerous tests have appeared on the market, which detect either the presence of the virus or the presence of antibodies against the virus. Both PCR and serology tests are becoming increasingly available as labs are scaling up their capacities. With a legion of assays available, many approved by FDA, and other regulatory bodies, the question arises which test will be the best to include in a study. The reliability, sensitivity and specificity of tests, are not always clearly demonstrated, documented or readily determinable. For this reason, Cerba's scientists have performed a comparative study for different assays and technologies and have drawn up a list of tests which meet certain minimum criteria. Seeing differences in the respective Sars-CoV-2 gene and its mutations present on different continents, the need arises for a sequencing approach. It is important to note that the classification of cases is a surveillance tool that can be used to better understand the burden of the disease, and moreover the treatment suited for a certain individual. The use of current tests will evolve as we are increasing our understanding of the virus itself and newer tests are becoming available.

Technology and Decentralisation as an Alternative

The landscape of clinical trials never ceases to evolve, and next to scientific breakthroughs, the COVID19 pandemic has revealed the urgent need for the next-generation technology-driven clinical trials.

Deviation from protocols is highlighting the risks of missing or delaying data collection from ongoing studies. This underlines the value of digital medicine, which is emerging by its advancements in cloud, mobile and IoT. Virtual trials are unfolding an extraordinary opportunity for pharma and healthcare, taking clinical trial management to a whole new level. It is very likely that virtual trials and digital healthcare will become more mainstream as part of the new 'normal' beyond COVID-19. There are numerous benefits to virtual trials, both short-term and long-term, though also limitations. Remote patient monitoring gives participants the freedom and the peace of mind they won't be exposed to unnecessary risks.

Virtual visits will allow the ability to reach a larger population of patients and will improve patient recruitment, engagement and retention. With the clinical trial ecosystem turned upside down, the emergence of virtual technology has the best chance to succeed and change the shape of clinical trials to be conducted for the coming years. Next to going digital, another solution to the current challenges includes deploying decentralised clinical trials, protecting both patients and medical staff. The FDA has published guidance back in March 2020 advising alternative methods while travelling to sites was heavily restricted, hence supporting the incorporation of decentralisation. For a couple of years now, some CROs as well as technology and software companies have been exploring this road of new patient-centric options. The COVID-19 pandemic has now paved the way for virtual trials and hybrid trials to become more widely accepted and perhaps eventually even become the norm.

Post-COVID-19: The Future is Now

We are witnessing a true transformation of the clinical trial process and at a pace hitherto unforeseen. For the last decade, whilst some solutions were deemed too risky, the risk of not implementing them now has become greater. Change in this industry is a matter of survival, and many of the changes that were made during the COVID-19 pandemic will last and be for the better.

Case Study – Speed and Efficiency Were of the Essence

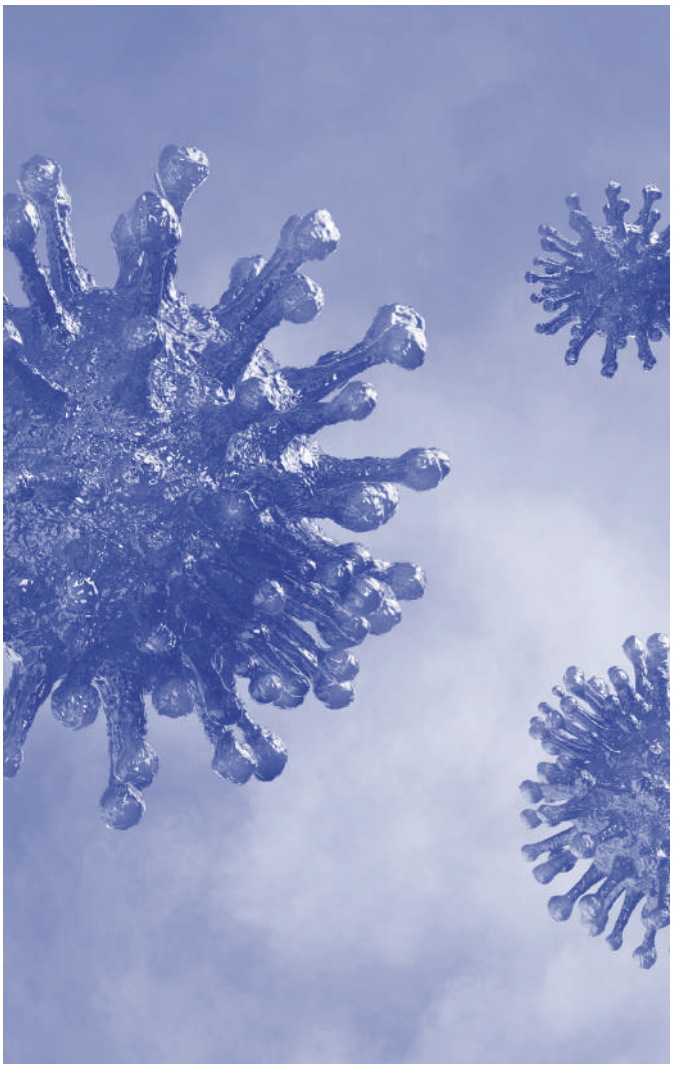
Cerba Research was engaged by the Belgian government to participate in a government-led consortium. Working with a large team of software providers, pharmaceutical companies, CROs, laboratories and research institutes, we developed an approach for collecting and integrating data, aggregating and correlating it into focused dashboards, and setting up a framework to make relevant operational decisions. After setting up the initial framework and dashboard within only one week, we have supported the task force's operational and scientific teams on a daily basis.

Led by the Federal Minister, the members of the task force worked (and are still working) to increase testing against COVID-19, an important tool in tackling the further spread of the virus, in order to flatten the curve. Cerba Research, the clinical trial & research division, with its headquarters in Ghent, Belgium, is providing the logistical support and organisation for this project, taking a pivotal role in the delivery of patient samples to pharma and academia for COVID-19 testing.

Key Achievements:

- Successful setup in only one week, including creation of a new database
- Sourcing materials in-house for shipments on time despite current logistical challenges
- Ability to quickly adapt to daily changes made and source new required supplies

Contingency planning and our flexibility to execute quickly and communicate effectively allowed us to meet all timelines. Risk identification and challenge mitigations proved helpful as the team were well prepared and showed an agile and determined mindset for this project.



Sofie Vandevyver

Sofie joined Cerba Research six years ago and holds a PhD in Science, biotechnology. She combines her contracts and proposals experience with her scientific background to function as the Cerba Research head of business operations & marketing.

Daniel Tanner

Daniel joined Cerba Research in 2018 having spent 15 years in the industry across several leading CROs in senior commercial roles. Daniel is Head of Business Development at Cerba Research.

Mario Papillon

Mario is CEO of Cerba Research. Mario joined the Cerba HealthCare Group as the CEO of Cerba Research (formerly Barc Lab) in November 2017. A pharmacist by training, Mario has more than 25 years of experience in the pharmaceutical, biotechnology, and CRO industries.