

## Commentary



# Clinical development and trial operations in COVID-19 era

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## INTRODUCTION

Coronavirus disease 2019 (COVID-19) pandemic affects worldwide and various aspects of human life, including drug developments and clinical trials. Especially in trial operations, there are significant impacts from 2020 to 2021. According to the Arkivum report [1], 'TMF futures 2021: good data within the age of digital transformation,' 41% of latest clinical trials in 2020 were delayed or placed on hold indefinitely because of the COVID-19 pandemic, 41% of those delayed trials will now be run in 2021, 65% of the life sciences sector say they will still run clinical trials remotely after the pandemic, 57% of the sciences organizations say the price of running a trial has increased since the pandemic began and 49% of the sciences organizations say the time to finish a clinical trial has increased since the pandemic started. We need to review the trends and possible changes during and after the COVID-19 pandemic reviewing the various reports from biopharmaceutical consulting companies and contract research organizations (CROs).

Here is the explanation of 10 trends and industry changes affecting clinical development and trial operations in the COVID-19 era.

## TEN TRENDS AND INDUSTRY CHANGES AFFECTING CLINICAL TRIALS IN 2021

### COVID-19 trials on the increase

The onset of a world health emergency in 2020 set multiple biotech companies during a race to develop and register a vaccine effective against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In keeping with the World Health Organization (WHO)'s COVID-19 Candidate Vaccine Landscape and Tracker, 129 coronavirus vaccines are currently being tested in clinical trials. With over 194 in pre-clinical stages (as of November 5th, 2021), it is clear that demand for vaccine trials will remain high, while several vaccines against SARS-CoV-2 were registered and marked already. Even in Korea, there are several vaccines against SARS-CoV-2, including early-phase to late-phase clinical trials. But due to the high vaccination rates, around 80% of completed vaccinated subjects, it is hard to enroll enough subjects in a single country.

High numbers of vaccine trials are influencing enrollment and begin-up periods. Logistics challenges affecting timelines and access to large populations may be solved by clinical trial services providers, who can give ready-to-plug-in infrastructure, including cold chain management and expedited timelines for gaining access into particular countries of clinical trial conduct [2]. Also, there are many clinical trials on oral anti-viral agents and it is very close to get the products soon maybe within the end of 2021 (e.g., molnupiravir from Merck & Co. Kenilworth, NJ, USA; a mixture of PF-07321332 and ritonavir from Pfizer, New York, NY, USA).

### Disruptions to clinical trials

The most apparent impact of the worldwide pandemic on clinical trials was the suspension of enrollment during times of high contagious risk [2]. In March 2021, GlobalData's Pharma Intelligence Center reported that over 1,200 clinical trials worldwide had experienced disruption owing to the COVID-19 pandemic. Alongside the problem of delayed timelines arose specific supply chain problems, including logistical challenges around the supply and transportation of biological samples and ancillary supplies for clinical trials. One of all the critical issues is a proper enrollment of patients, especially patients with cancers and rare diseases. Usually, they are the vulnerable population of COVID-19 infection. The long-term impact is connected to using the simplest practices developed during COVID-19 changes. Remote monitoring was always a top discussion topic, but it absolutely was never utilized within the best way. Right now, CROs are being forced towards building infrastructure and technologies required to support things like direct-to-patient logistics. These will still be used after COVID-19. Companies were required to reply quickly and effectively to the newly found challenges and restrictions to keep the clinical trials running during lockdowns.

### Sudden increase of remote trials

When the remote trial model witnessed sudden and increased deployment, significant changes occurred to the traditional clinical supply chain. Direct-to-patient approaches provided an answer to the varied logistics requirements of remote trials, with service providers acting because of the bridge between sponsors and patients [2]. But in countries such as Korea, it is difficult for the sponsors or CROs to provide that kind of service because of regulation. With decentralized trials, global reach is more easily achievable for trial sponsors. This includes even the main distant sites where patients are located. Despite the enormous opportunities, this presents for clinical research in terms of expanded participant pools, challenges concerning dynamic regulations and the changing requirements for every location become issues for sponsors attempting this approach. There are also challenges of dealing with medical regulations (or sometimes the absence of such regulations) that cover delivering drugs to patients.

CROs are up to now with all the local requirements and are able not only to follow the regulations, but to shape it during a particular frame to render and enable a much better environment for decentralized clinical trials with adaptive clinical trial designs and remote monitoring using information technology. The pandemic might have rushed such trials into adoption, but demand will remain high long after COVID-19. CROs are thus watching developing web and mobile applications for direct-to-patient logistics if the regulation permits.

### Increased target precision dosing and monitoring of specialty drugs

Adverse drug events (ADEs) cause quite 770,000 injuries or deaths in U.S. hospitals every year, in step with a study within the *Journal of Informatics in Health and Biomedicine*. Such adverse events prolong hospital stays by up to 4.6 days and add a value burden of over \$30 billion annually to the U.S. healthcare system [3]. Because the effort continues to reduce harm

from ADEs, the industry will start to determine a rise in precision dosing and monitoring of specialty drugs, especially for those with narrow therapeutic indexes and wide variations in drug response. It anticipates that pharmaceutical companies will place an early emphasis on precision dosing during clinical trials associated with drug development. It is a paradigm shift in continuous efforts to ultimately improve care and reduce healthcare costs.

### Expanded access programs and post-trial monitoring

Through expanded access programs, patients outside of clinical trials who have severe, life-threatening conditions can obtain access to investigational therapeutics when alternative treatment option is not satisfactory. European Medicines Agency (EMA) recommends that run participants should be ready to continue the investigational treatment they received in the clinical trial [2].

The marketplace for post-trial monitoring of this sort is growing as post-trial responsibilities increase for sponsors. But still, there are some concerns from nongovernmental organizations and citizens that this kind of expanded access programs may be considered marketing activities of the sponsors and abused from time to time.

### Digital transformation for oversight of clinical trials

Digitization may be a trend affecting every industry going, and clinical trials also are not the exception. The 21st century has seen the event of various digital technologies that facilitate the gathering, managing, and analyzing of clinical trial data. Software platforms help the sponsors achieve a more efficient, transparent process of clinical trial management. They create it easier for stakeholders to access accurate study information from digital devices, improving decision-making and protocol following on time. The introduction of Internet of Things devices like smart sensors, wearables, and connected medical devices are utilized to collect physiological data of trial subjects, leading to real-time monitoring, greater accuracy and richer data sets so as to foster the clinical development of innovative new drugs [4].

Main area for digital transformation is as follows [5];

- Decentralized trials
- Digital endpoints
- Data analytics and visualization
- Data strategies
- Patient-centric trials
- Evolution of information management

### Pressure will mount to unblock run bottlenecks

The COVID-19 pandemic has underscored the requirement to optimize clinical trial processes. While the public-private initiative Operation Warp Speed of the U.S. has won public attention for its ability to expedite and facilitate vaccine development and distribution, it is also focused new attention on common bottlenecks within the clinical trial process and operation [3]. The industry is looking at steps the life sciences industry could take to remove those bottlenecks and speed up the process for new innovative drug candidates.

Some expert [6] cites several strategies to optimize clinical trials, including exploring new access points for patients, using artificial intelligence (AI) to compress the screening process, generating public awareness of the advantages of participation, encouraging physicians' participation, and expanding patient diversity.

### Radiomics will get ahead in drug development and clinical trials

The definition of radiomics is the method that extracts an outsized number of features from radiographic medical images using data-characterization algorithms. Precision imaging analytics technology will see increased adoption from 2020 and can be incorporated into drug development strategies and clinical trials management. These AI-powered analytics will enable drug developers to realize deeper insights from medical images and drive accelerated development of efficacious treatment, better-personalized treatment, and therefore the discovery of novel biomarkers that may enhance clinical decision-making and treatment [3].

### Priorities for drug developers will continue to shift

From 2021, drug developers' priorities will still evolve in meaningful ways. The industry will see continued growth in streamlined research for drugs and understanding pathogenesis, diagnosis, and treatment options of rare diseases. We expect to watch the growing interests of “nichebusters” instead of the old-fashioned blockbuster model. The life sciences industry is watching unmet needs and developing drugs to handle these. While the “nichebusters” concept has some successful history, still growing progress in precision medicine will make it easier for pharmaceutical companies to make sure they need the proper patient or patient population for their targeted drugs or therapies [3]. As the number of medicines entering the market increases with pricing and market-access pressures, including listing and insurance coverage. Pharmaceutical companies' ability needs to improve for value-based assessments supported by real-world evidence to enable drug access, product brandings, etc. But still, regulatory agencies and governmental organizations show the concerns to use real-world data to replace well-designed clinical trials and health economic studies. Hopefully, the real-world evidence will support the market access of innovative and expensive new drugs.

### COVID-19 will still surprise

For all of the brainpower and data models researchers have accustomed to model the COVID-19, the pandemic continues to surprise experts [3]. The unprecedented nature of the pandemic makes it challenging to anticipate what impact the virus will have next year. There is enough information now to try and do future estimates. There are numerous unknowns.

## SUMMARY

1. From 2020 to 2021, the life sciences industry has felt an irrevocable change. After 2021 there will be more focus on further enhancement of technology with providing from sponsors, service providers, and patients.
2. There is no going back. The industry is totally able to evolve and involve patients in ways never seen before, resulting in better clinical trials, better treatment options, better clinical outcomes, and better patients' lives.
3. From 2021 and beyond, it is expected to work out data professionals embracing new technologies, new endpoints and new tools to attain the important goal—bringing life-changing therapies to patients safer, faster, smarter, in an innovative and cost-efficient manner through new approaches to clinical development and clinical trial operations.
4. Korean pharmaceutical industry should be more proactive in engaging new technology and patients to develop innovative medicine in the era of COVID-19 and after the pandemic. Efficiency is one of the capabilities, but creativity and flexibility will be the primary driver in this critical period.

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