ROUNDTABLE SUMMARY

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Infectious Disease Clinical Trials: Navigating Innovation & Rising Complexity

Chijioke Bennett, Senior Director, Clinical Development, Novavax
Grace Chen, Vaccine Development Consultant
Nele Langenaken, General Manager, Cerba Research
Trina Racine, Director, Vaccine Development, Vaccine and Infectious Disease Organization (VIDO)
John Rex, Chief Medical Officer, F2G
Roxana Rustomjee, Senior Director, Clinical Development, Infectious Diseases, BioNTech

Moderator: Janelle Hart, Managing Editor, Custom Content, Citeline

KEY TAKEAWAYS

- Infectious disease R&D sped up during COVID-19, but timelines and funding are now returning back to normal levels.
- Operational barriers to infectious disease clinical trials persist.
- To accelerate vaccine development timelines, sponsors and sites need better surveillance and communication.

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OVERVIEW

Following the trials and tribulations of COVID-19 vaccine development, the infectious disease landscape is advancing rapidly. Now more than ever, the life sciences industry is experiencing major scientific and technological innovation that has the potential to dramatically enhance infectious disease R&D in the future.

The challenge is keeping up with that innovation. It is imperative that pharma and biotech decision-makers develop strategies that will ease the integration of novel technologies and robust clinical approaches into existing R&D workflows, all while taking regulatory considerations and market complexity into account.

CONTEXT

The panelists discussed the evolving landscape for infectious disease clinical trials, the operational barriers for therapeutics and vaccine development, and why improving epidemiologic surveillance and communication are critical to strengthening site and patient enrollment in clinical trials.

KEY TAKEAWAYS

Infectious disease R&D sped up during COVID-19, but timelines and funding are now returning back to normal levels.

In the wake of COVID-19, the landscape for infectious disease research has been dominated by innovation across treatment modalities. The funding and accelerated approvals that supported research during the COVID period infused the space with excitement and optimism. Interest in respiratory viruses, for instance, has especially heightened with focused attention on developing a combined vaccine.

> "Everybody is talking about, 'We're going to have only one shot for RSV flu and COVID.' That's the buzzword now."
>
> *Nele Langenaken, Cerba Research*

As the hype surrounding COVID and respiratory viruses dissipates, there is concern in the infectious disease community that some of the momentum and funding that flowed into therapeutic and vaccine development research during the pandemic may be tapering off. The panelists noted, however, that there remain significant medical needs from a host of diseases. Developing therapeutics for these unmet medical needs warrants continued attention and support from the research community, as well as continued funding.

> "During COVID, all the forces of good came together but in a world with so much medical need, we might soon have to move that attention someplace else. The wise thing to do is to ride the coattails of whatever advances we've made . . . but don't expect this heightened frenzy to be the new normal—it has to dissipate, but hopefully not to pre-pandemic levels."
>
> *Chijioke Bennett, Novavax.*

Despite helping combat the pandemic and exciting researchers about new R&D possibilities, the rapid development of COVID-19 vaccines reverberated in a negative way among some parts of society. The voices of anti-vaccine advocates, who have stirred the flames of vaccine hesitancy for a long time, became louder and spread the idea that the COVID vaccines could not be trusted because they were developed too quickly. Vaccine distrust then spread to other areas and started impacting pediatric vaccine uptake.

With that in mind, as the industry turns to other areas of unmet medical need, it shows the importance of constantly working to build and maintain public trust.

Operational barriers to infectious disease clinical trials persist.

Despite the pandemic-driven spike in infectious disease R&D and accelerated timelines for therapeutics and vaccine development—which made it seem like the industry is recalibrating for the better—operational challenges remain.

One challenge is unrealistic expectations for clinical trial timelines created during COVID. The speed at which COVID trials were conducted is not achievable under normal conditions and is impossible for all but the largest pharma organizations. "We are an academic-based organization, so our funding levels are much smaller, yet we are still expected to meet the same standards as large pharma organizations," Trina Racine, director, vaccine development at VIDO, said.

Other operational barriers include site contracting, subject recruitment and sampling, and activating clinical trials, which is still a lengthy process, especially in Europe, where institutional review boards now take up to six months to approve trials.

> "It is maddening to think about those kinds of delays. It has certainly not gotten better, though briefly [during COVID] everybody in the world pitched in to solve the problem while developing specific vaccines."
>
> *John Rex, F2G*

There are also challenges related to the lack of staff and resources needed to conduct large trials. Sites are reluctant to relinquish the processing of samples to centralized labs that use standardized equipment due to their preference for end-to-end control of R&D.

"As sponsors, in our conversations, we need to bring to the table the sites and get their buy-in on using central vendors," Chijioke Bennett, senior director, clinical development at Novavax, said. He and Nele Langenaken, general manager, Cerba Research, both highlighted the difficulties that vaccine manufacturers had run into during the pandemic while receiving test result data from multiple sites, each using their own equipment to validate assays.

> "Decentralized testing for infectious diseases was a big thing, but it has died as fast as it came up after the pandemic. It's very expensive compared to testing done at sites and people are not that interested in waiting at home for a nurse to come and collect their samples. [The pharma industry] wanted to make it work, but it wasn't thought through."
>
> *Nele Langenaken, Cerba Research*

Other operational challenges linger on as well, resulting from the industry failing to dismantle some of the exceptional measures it took to compensate for the impact of COVID on the clinical trial landscape. "The markup for a clinical trial post-COVID has remained at around 50% of what it cost pre-COVID. That has remained without the emergency situations that originally motivated that markup," Roxana Rustomjee, senior director, clinical development, infectious diseases at BioNTech, said.

Lastly, one *anticipated* barrier is the enormous "unknown" of how well the industry and regulators will be able to integrate AI tools and concepts into infectious disease R&D processes. "During COVID, BioNTech had to ramp up its use of AI systems, electronic connectivity, and AI-facilitated decision-making," Rustomjee recalled. Going forward, though, it is unclear whether that pace of adoption can be shared and maintained across other biopharma companies and the FDA.

> "It will be interesting to see in the next decade how AI gets built into end-to-end discovery-to-licensure and how much of that data regulators are willing to accept."
>
> *Chijioke Bennett, Novavax*

Infectious disease therapeutics

In addition to these common operational barriers for clinical trials, research in infectious disease therapeutics faces some specific challenges. One of them is a reluctance on the part of medical centers to specialize in—and develop a reputation as centers of excellence for—drug-resistant bacteria.

> "The consequence for development is that if you want to develop a therapeutic for a multidrug-resistant pathogen, you have to do it in the setting of what I sometimes call 'usual' drug resistance."
>
> *John Rex, F2G*

The limitations that come with working with small datasets, which are typical in the antibacterial and antifungal therapeutics space, represent another operational barrier. In addition, the economics of developing new antibiotics, which under current reimbursement models are not favorable for companies' bottom line, are yet another hurdle.

The PASTEUR Act, which is hoped to be passed by Congress this year, aims to address that hurdle by authorizing the US government to purchase a small number of novel antibiotics addressing key unmet needs per decade and stock pharmacies nationwide with them. "The antibiotics would be bought as if they were fire extinguishers—you pay for them, you install them in the pharmacies, you look at them each day, and you say, 'I'm delighted that that's there and I'm also delighted that I don't need to use them to treat an infection today,'" John Rex, chief medical officer at F2G, explained.

Infectious disease vaccines

Like the infectious disease therapeutics space, the infectious disease vaccine development space also faces some barriers. Challenges can include navigating the types and quantity of data required to get regulatory approval for use in humans.

Rustomjee called for the need to "push the envelope" in urgent circumstances, which can include rare diseases. She cited examples where licenses have been granted based on small and unique datasets, including data from animal models. What is necessary in such circumstances are active conversations between vaccine developers and regulators.

Another challenge is waning public interest in participating in vaccine trials, in part due to antivaxxer-fueled vaccine hesitancy and COVID-related exhaustion.

"If we could educate populations before they enter a trial and enable [stronger] community engagement, perhaps we could retain more people into vaccine studies," Racine said. She based her observation on a Phase II trial her company had run in Uganda, where liaison groups were going into local communities, explaining the purpose of the trial and the vaccine being developed, and positively motivating people to participate in the study.

> "I found retention to be much higher in Uganda versus in North America, where anybody off the street can sign up, but also decide that once they've had their first dose, they're not going to follow up."
>
> *Trina Racine, VIDO*

To counter that North American trend, as well as vaccine hesitancy in general, it is important that clinical site staff know how to level with trial participants. For example, when Bennett went to get vaccinated in 2021, the police officer directing traffic to the vaccination site—who was Black, like Bennett, and seemingly not accustomed to seeing many Black individuals getting the vaccine—asked him whether he thought the vaccine was safe. He took that as an opportunity to casually educate her and instill confidence in the vaccine's safety.

> "Part of having a successful clinical trial is learning how to speak to the person on the street corner. We have to do what the politicians do – go grassroots. Ask them to tell us what their concerns are."
>
> *Chijioke Bennett, Novavax*

On top of the obstacles mentioned, vaccine developers are experiencing difficulty in assessing efficacy due to the interfering effects of COVID, which has led to atypical flu and RSV strains.

> "This is where vaccine developers need to lean in to established laboratory networks for peripheral blood mononuclear cell (PBMC)—a critical factor to understanding vaccine effectiveness."
>
> *Nele Langenaken, Cerba Research*

> "In COVID, the risk/benefit analysis is a little bit different than maybe in other diseases, but we're definitely seeing an impact of COVID."
>
> *Grace Chen*

To accelerate vaccine development timelines, sponsors and sites need better surveillance and communication.

In the context of vaccine development for infectious diseases, better public health surveillance means having a full view of any outbreaks or pockets of rising infection rates happening anywhere. Unfortunately, that is frequently not the case.

> "We would like to be able to conduct studies where the disease is more prevalent and potentially most clinically meaningful and severe. But it's hard to find sites if [your site or network of sites] doesn't see the disease, while the site sitting next to you does. Diseases of interest to public health happen in many places but we don't all have the same level of surveillance."
>
> *Grace Chen*

Support for faster enrollment and completion of vaccine clinical trials can also come from changing the way sponsors communicate the utility of vaccines. As members of the scientific community, researchers tend to hedge their communications using science-speak (i.e., "What I know right now will change as more evidence comes along"), but the average citizen has no intuition for such nuances.

> "We have to do better at presenting ourselves, presenting the data, and somehow shutting down those super confident antivaxxers."
>
> *Trina Racine, VIDO*

Beyond surveillance and communications, there is a role for regulatory agencies, as well. With the goal to develop a combined vaccine that contains a bundle of antigens and protects against several pathogens at once, regulators may need to revise conventional expectations that safety and efficacy claims must be demonstrated for each pathogen in isolation. Enacting revisions, updating regulatory submission guidelines, and then harmonizing them globally—something that is already happening on a regional level in Africa—can go a long way toward improving R&D.

> "Regulation has to keep pace with the speed that is being asked for."
>
> *Roxana Rustomjee, BioNTech*

Last but not least, AI's expanding capabilities will likely enable companies and public health bodies to predict emerging pathogen strains, but this will only be useful if organizations are equipped to respond to such threats before they spread. The outlook is that the incorporation of AI for those purposes will take a long time, just as getting quantitative polymerase chain reaction testing widely accepted did.

CONCLUSION

Going forward, in the infectious disease space, innovation in manufacturing and the transition from bench science to manufacturing are expected to play an increasing role in the overall R&D process. Many of the most innovative therapeutics come from small biopharma companies, yet those companies are at a disadvantage in terms of resources and scale compared to their larger and more established peers; building strong relationships with manufacturers and finding ways to streamline critical processes such as antigen selection will be critical success factors for them.

> "What we're trying to do with our internal scientists is educate them as to what is required of their discovery research to make the transition into process development and those first clinical lots easier. If the scientists can start thinking about those aspects during early discovery, the hope is that the transition to process development and GMP manufacturing will be easier and cheaper."
>
> *Trina Racine, VIDO*

> "One 'good' thing about COVID is that the understanding that you can die from an infection has changed the way we get people's attention. At a political level, we now have politicians who can say the words 'antimicrobial resistance' and people understand those things at a deeper level."
>
> *– John Rex, F2G*

BIOGRAPHIES

Chijioke Bennett

Senior Director, Clinical Development, Novavax

Dr. Chijioke Bennett (MD, MPH MBA) is Senior Director, Clinical Development with the responsibility of leading clinical development programs for the COVID variant vaccines and COVID vaccines in immunocompromised populations. He also lends his clinical development leadership support to the COVID/Flu combination vaccine work. He is a clinical research physician and biotech executive with training and expertise in general medical practice, global public health, clinical research, epidemiology, health policy, health disparities, health economics, health leadership, and business administration across multiple continents. With over a decade of diverse experience across multiple specialties, and in multiple industry roles, he has helped develop and lead global clinical trials in stem cell research technologies and now in infectious disease vaccinology, where he brings to bear all the experience, he has garnered over the years leading and supporting multiple cross functional teams.

Grace Chen

Vaccine Development Consultant

Grace Chen is an Infectious Disease physician who received her MD from George Washington University and completed her Internal Medicine Residency at Beth Israel Deaconess Medical Center in Boston and an Infectious Diseases Fellowship at the National Institutes of Health. She began her career in vaccine development at the NIH where she evaluated live attenuated pandemic influenza vaccine candidates in preclinical and phase 1 studies. Subsequently, Chen joined the Vaccine Research Center at NIH where she served as principal investigator on multiple phase 1 clinical trials across a breadth of pathogens and vaccine platforms and also served as Deputy Chief and then Chief of the Clinical Trial Program at the Vaccine Research Center overseeing the entire clinical portfolio of phase 1 and phase 2 studies. Chen subsequently joined Moderna Therapeutics in 2021 to oversee the clinical development of RSV vaccine for older adults. The statements expressed at the Roundtable are Chen's personal opinions and not associated with her affiliation with any current or former organization.

Nele Langenaken

General Manager, Cerba Research

Nele Langenaken has over 25 years of experience in the Central Lab & Testing industry. She joined Cerba Research in 1998 and has founded Cerba Research US in 2001 of which she is still the General Manager. She holds a Bachelor in Science from the Ghent University. Nele is responsible for ensuring the smooth operational and scientific coordination of clinical trials on behalf of sponsors globally.

Trina Racine
Director, Vaccine Development, VIDO

Dr. Trina Racine possess a PhD in Microbiology and Immunology from Dalhousie University (Halifax, Nova Scotia, Canada) and is currently the Director of Vaccine Development at VIDO.

Upon completion of her PhD, Racine joined the Special Pathogens Program at the National Microbiology Laboratory (NML), part of the Public Health Agency of Canada. While at the NML Racine worked on the development of vaccines and therapeutics for various emerging and re-emerging infectious diseases, including Ebola, Zika and MERS. Racine coordinated clinical trials and provided diagnostic support to the Ebola outbreak in West Africa in 2014-2016. Prior to joining VIDO, Racine was a Scientific and Regulatory Affairs Consultant for GeneOne Life Science, Inc., a South Korean based biopharmaceutical company.

As Director of Vaccine Development at VIDO, Racine is responsible for guiding the development, manufacturing, and clinical/field testing of VIDO's internal products using a Stage Gate process. Racine is also responsible for VIDO's Vaccine Development Centre (VDC), a pilot scale, Containment Level 3 capable, GMP biomanufacturing facility capable of producing veterinary vaccines to North American licensure and human vaccines to Phase II clinical trials.

John Rex
Chief Medical Officer, F2G

John H. Rex, MD, FACP is a physician and drug developer with more than 35 years of development and policy experience focused on antimicrobial agents. He is currently CMO for F2G, Ltd. (an antifungal biotech), is an operating partner with a venture capital group (Advent Life Sciences), is Chair of the Scientific Advisory Board of the $1b AMR Action Fund, and was (2015-2019) a voting member on the US Presidential Advisory Council on Combating Antibiotic Resistant Bacteria (PACCARB). He also blogs regularly at http://amr.solutions/blog.html.

His experience includes moving compounds from preclinical development through all development phases via academic positions (NIH, Bethesda, MD; McGovern Medical School-Houston) and VP-level roles at a multinational pharmaceutical firm (AstraZeneca). Other past activities include advancing novel regulatory paradigms for antibacterials, publications on novel reimbursement models for antibiotics, co-founding of a public-private partnership (CARB-X), co-founding the New Drugs for Bad Bugs (ND4BB) program of Europe's Innovative Medicines Initiative (IMI), and a 4-year term as Industry Representative on the FDA Anti-Infective Drugs Advisory Committee (AIDAC, 2007–2011).

Roxana Rustomjee
Senior Director, Clinical Development, Infectious Diseases, BioNTech

Roxana Rustomjee is an infectious disease physician, epidemiologist and public health specialist leading a team of scientists to advance development of vaccines through all stages of development, registration and achieving reimbursement; for vaccines that have weak financial investment incentive but high unmet need. A leader with a focused and driven personality, more than 20 years in global R&D leadership roles ranging from academic research; public-private sector product development partnerships; government agencies and the pharmaceutical industry on vaccines, drugs and diagnostics.

Janelle Hart
Managing Editor, Custom Content, Citeline (Moderator)

Janelle Hart is an experienced writer and editor with a background in health care communications and journalism. She currently produces sponsored content across an array of mediums and platforms that focuses on pharmaceutical and biotechnology news and insights. In addition, she contributes to Citeline's unsponsored content, such as Scrip Asia 100, Outlook and In Vivo's Rising Leaders series. Hart received a dual bachelor's degree in English and Media and Culture from Miami University and is currently pursuing a master's degree in Publishing and Writing from Emerson College in Boston, where she currently resides.