CenterWatch Weekly

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‘Snapback’ to Pre-Pandemic Trial Approaches Unlikely, Focus Is on Innovation

By James Miessler

As the return to normalcy continues in the post-COVID-19 pandemic world, a new state of the industry report shows that most sponsors and CROs intend to continue using innovative measures adopted during the health crisis and believe such approaches are here to stay.

The report, based on a survey by WCG’s Avoca Group, showed that decentralized trial and patient engagement innovations, for example, had already seen interest or increased use prior to the health crisis, but responses varied widely depending on the type of innovation. Most surveyed believed that adapting to the pandemic had had a positive effect on clinical research and trial quality.

“There was very widespread agreement that the pandemic had been critically impactful or very impactful in actually improving the research model in a sustainable way for the whole industry,” said Denise Calaprice, a senior consultant at WCG Avoca. “For every innovation, every category of innovation and every aspect of quality we asked about, most people felt that the impacts on quality had actually been positive rather than compromised. Interestingly, even though implementation was lowest and there was concern about lack of understanding it, some of the most positive perceptions were use of artificial intelligence (AI) in protocol and clinical development and design planning.”

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Despite Pandemic Positives, Crisis Highlights Issues with Growing Use of Service Providers

By James Miessler

The COVID-19 crisis showed sites that sponsors and regulatory agencies are capable of moving at unprecedented speed to respond to trial and protocol adaptations. But the pandemic has also revealed some problematic issues, including a growing reliance on technology and service vendors and the siloing of different partners in the trial process.

Sites have expressed amazement at the fast pace sponsors and regulatory agencies have demonstrated in their responses to trial changes during the pandemic, as well as pleasure at being able to give patients greater choice, convenience and access to trials, says Ken Getz, director of the Tufts Center for the Study of Drug Development.

But sites are operating with “an even more fragmented and siloed set of partners that have to be trained and brought up to speed, where we do not see a high level of coordination and integration, where there’s a lot of uncertainty, and that has contributed to the higher potential for errors and mistakes,” Getz said. “Based on comments from sites, it’s also contributed to delays in receiving clinical supplies and lab kits as well as even receiving payments for work that’s been performed.”

These vendors and partners must be qualified by sponsor companies to be used for a clinical trial, a process that is

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Industry Briefs

Biden Administration Lays Out Goals for Potential FDA Regulations

The Biden administration has released its first unified agenda of proposed regulatory actions, a set of goals that include rules to synchronize FDA regulations with requirements of the Common Rule.

The unified agenda, which is published twice annually and is by no means set in stone, features three rules that involve IRB regulations.

One proposed rule would require any institution doing multisite cooperative research in the U.S. to get approval by a single IRB for research conducted in the country, though it notes there are some exceptions. The proposed rule would also require IRBs to keep records of research that takes place at an institution where IRB oversight is conducted by an IRB not run by that institution. The rule, which has a notice of proposed rulemaking set for December, represents the FDA's harmonizing with requirements of the Common Rule, which was last updated in 2018.

Another proposed rule, vaguely described, looks to harmonize other certain provisions of the FDA's regulations on human subject protections and IRBs with the Common Rule. It would also make minor amendments to "related regulatory provisions," though the rule does not give any detail on which provisions it would target. It also has a December target deadline.

The third, a final rule with a February 2022 target date, would establish an FDA regulation allowing IRBs to waive or alter certain informed consent elements or to waive requirements to obtain informed consent under limited conditions, though only for "certain minimal risk" clinical trials. Its goal is to facilitate certain minimal risk trials to support the development of new medical products. The regulation had already been mandated by the FDA through a guidance issued after the Common Rule was updated.

Read the entire FDA/HHS rulemaking agenda here: https://bit.ly/3iSLg5Z.

NIH Commits to Combating Structural Racism in Biomedical Science

The NIH has come out with a strong commitment to ending structural racism in the biomedical research field, outlining its long-term goals and initial actions in its ongoing push for racial equity.

In a new commentary published in *Cell* by NIH Director Francis Collins and other officials, the institute reaffirmed that structural racism is a chronic problem that has managed to find its way into biomedical research. The institute noted its diversity and inclusion programs have been "valuable but not sufficient."

The officials detailed the progress of an ongoing initiative, UNITE, which seeks to identify and address structural racism in the scientific community by increasing inclusivity and diversity, establishing an "equitable and civil culture" in biomedical research and tearing down barriers to racial equity in the biomedical research workforce. The program was established in March, and NIH staff have been engaging in research to identify opportunities, make recommendations and employ strategies that increase the inclusion of minorities.

Efforts thus far include an increase in funding opportunities for projects that look to understand and address the impact of racism and discrimination on minority health and health disparities; expansion of the NIH's diversity and inclusion programs for hiring senior trial investigators; enhancing recruitment of candidates from underrepresented groups and improving retainment rates for diverse staff; gathering demographic data for staff across all NIH job areas and sharing that information; and evaluating policies and practices that may contribute to perpetuating structural racism.

For example, the institute said it has already met its goal of obtaining support for a grant by the National Institute on Minority Health and Health Disparities centered on the impact of structural racism and discrimination on health equity. It has also completed its target of publishing a request for information on practical and effective ways to improve the racial and ethnic inclusivity and diversity of research-centered environments and staff. An effort to appoint high-level staff members that will work to improve diversity, equity and inclusion at each NIH institute and center is already underway, among other measures, the NIH said.

The NIH has established multiple offices focused on improving diversity, including its recently created Equity Committee, which systematically tracks and measures diversity and inclusion metrics for each NIH institute and center's intramural research program.

Read the full commentary here: https://bit.ly/3gkUaHZ.

Firms Name Clinical Research the Most Expensive, Delay-Prone Aspect of Business

A majority of biopharma professionals deemed clinical research to be the most expensive part of their business and the area of drug development with the most bottlenecks, but they've taken different approaches to pursuing cost efficiency, a survey found.

Most professionals who responded — 57 percent — said that clinical research was the most expensive component of their businesses. By contrast, the second most frequent response, drug discovery and development, only came in at 16 percent as the priciest stage.

Forty-five percent of those surveyed said that clinical research was also the drug development stage in which they saw the most bottlenecks, while 22 percent of respondents said that they encountered the most snags during drug discovery and development.

The 113-person survey was conducted in May by Informa Pharma Intelligence and Cambrex.

Read the full survey report here: https://bit.ly/3gC4nzH.

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Trial Approaches

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According to those who responded, the innovations most likely to have been picked up in response to COVID-19 included shipping clinical supplies to patients' homes (47 percent), conducting study visits by telemedicine (40 percent) or home healthcare providers (32 percent) and hybrid trials (33 percent).

Conversely, a number of innovations were found to have been already adopted or eyed with interest before the pandemic hit, including electronic patient diaries (76 percent), online patient communities (58 percent) and the use of wearable sensors (57 percent). Ninety-four percent said they had already adopted or intended to incorporate visits via telemedicine into the trials, while 49 percent said they had no plans to work toward conducting completely site-less trials.

Most respondents, asked what they thought about the impact of such innovations on trial quality, believed decentralized activities would help retain and diversify study participants and support the streamlining of clinical development programs. Around one-quarter felt that decentralization could create significant risks to protocol compliance, participant safety and participant privacy.

A number of data/risk management and monitoring innovations had begun seeing use prior to the pandemic, including risk-based monitoring and study management tools (70 percent) and centralized remote monitoring (50 percent). But a number of tools were adopted by companies in large part due to pandemic restrictions, including remote reviews of source data (45 percent), remote verification of source data (41 percent) and remote reviews of electronic investigator site files (40 percent).

"For every innovation, every category of innovation and every aspect of quality we asked about, most people felt that the impacts on quality had actually been positive rather than compromised."

—Denise Calaprice, a senior consultant at WCG Avoca

Of the respondents, nearly all — 97 percent — had adopted or planned to adopt remote reviews of source data, but 58 percent said they had no intentions of leveraging AI to detect possible unreported adverse events, the survey found. Most respondents felt that innovations in the category aided data completeness and accuracy, protocol compliance, study data interpretations and participant safety, although more than 15 percent of them raised concerns about risks to participant privacy and the amount of human and financial resources that could be necessary.

Innovations in those two categories were the most likely to have seen use in response to COVID-19. On the other hand, innovative use of AI was spurred only on a small scale by the pandemic, with zero to 20 percent reporting they adopted certain AI-based innovations because of the crisis. Despite the relatively low adoption rates, most of those surveyed felt that such technology had a largely positive impact on trial quality, viewing the category as benefiting data completeness and accuracy, data interpretation, protocol compliance, the streamlining of clinical development programs, and the retention and diversity of participants. By comparison, only a few respondents felt the technology posed significant risks to trial quality.

The use of nontraditional study designs and endpoints were also only adopted on a small scale during the pandemic, with only 5 percent to 15 percent taking up such approaches. Around half of the respondents felt the innovations had a neutral impact on most trial quality aspects, while most of the remainder felt they had a positive effect. Thirty-two percent of respondents, however, felt that nontraditional study designs and endpoints could negatively impact the ability to interpret study data.

All respondents, including ones whose companies had not begun using nontraditional study designs and endpoints, cited regulatory concerns as the primary barrier toward effectively bringing on board such innovations, the report said.

Read the full report here: https://bit.ly/3cRtaOi.

Features

Crisis Highlights

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time-consuming and labor-intensive, not to mention expensive and inefficient, Getz said during a CenterWatch webinar last week on how to accelerate trial timelines.

The long qualification process involves an initial request for information (RFI), a formal request for proposal (RFP) process and a full qualification assessment, followed by a final contracting phase and master service agreement process. A Tufts CSDD study found that the process takes four to six months on average, with strong variation depending on whether it is a single-service provider or multiservice provider being qualified. The time it takes also varies by sponsor company size, with small companies generally being slower in the upfront areas of the process but faster in the contracting phase, and large firms conversely moving quicker in the beginning stages but slower in the contract segment.

Today, there are an estimated 3,300 to 3,500 CROs, full-service and niche-service providers, as well as approximately 1,600 technology services providers, that are contracted by sponsors to assist in clinical trials. The process to qualify them is estimated to cost sponsor companies between $375 million and $400 million dollars per year, Getz said.

"This is overall a very time-intensive and inefficient process," he said. "Requalifications are typically not significantly faster than qualifications, though you would expect them to be, given the fact that the sponsor now has more experience with a particular vendor or service provider. We hear from vendors today that this time-intensive process has really overburdened them and there are many vendors who do not have the capacity to continue to support such a high volume of RFIs and RFPs and qualification assessment activity."

"Our cycle times are getting longer and our practices in general, our experiences, are less consistent now than they have been in the past."

—Ken Getz, director of the Tufts Center for the Study of Drug Development

Jay Turpen, head of client services at Diligent Pharma, spoke further on the growing use of vendors in trials. While the new capabilities enabled by contracting with vendors are necessary given the technology advances the industry has seen, sponsors should take a thoughtful approach to managing and picking vendors early in the trial planning process, he said.

"It's really important through this new paradigm of all these companies collaborating that we think about, 'what does it mean to be a team?'" he said. "We really need to bring in all the players within a company, within a pharmaceutical company as well as all of the provider personnel, and really bring them together with cross-functional and cross-company planning, ultimately establishing the relationships that are going to be necessary to execute this clinical trial as quickly as possible."

Turpen said it's increasingly challenging to reduce the amount of time it takes to complete vendor qualification. And a number of companies have created a niche business of providing vendor qualification services from start-to-finish for sites and sponsors.

Getz also highlighted the overarching issue of growing trial complexity, an ongoing development that's contributed to slower cycle times. Overall, drug development durations have increased over time, and there has not yet been a single point where duration has shortened or accelerated, he said, noting that it now takes about 90 months to move a development program through first-in-human trials to regulatory submission.

An example of increased complexity can be seen in the average total number of endpoints in phase 3 trials. According to Tufts CSDD, phase 3 trials had seven total endpoints on average in 2005, a number that's spiked dramatically to 22 in 2020. Similarly, trials had 110 total procedures, on average, in 2005, a figure that's now more than doubled to 263 in 2020. And phase 3 trials now have 3.56 million data points on average as of last year, a massive increase from 2005's 494,000.

"Our cycle times are getting longer and our practices in general, our experiences, are less consistent now than they have been in the past," Getz said. "Our complexity and customization in our research activity is inversely related to performance. The more complex our activity, the more customization and the fragmentation supporting that customization all contribute to longer cycle times, higher dropout rates [and] a larger number of substantial amendments that are unplanned and unbudgeted."

Getz predicted that complexity and customization in trials should be expected to continue their rise. Cycle times, success rates and development costs should also be expected to worsen unless the industry finds new, effective ways to manage a more hybrid operating environment. A number of strategies are already being tested or implemented with the aim of creating more agility and flexibility, including the use of integrated systems, modified or flexible SOPs and staff that are trained to manage multiple technology solutions simultaneously, he said.

Drug & Device Pipeline News

Company	Drug/Device	Medical Condition	Status	Sponsor Contact
Asieris Pharmaceuticals	APL-1202 in combination with BeiGene's tislelizumab	neoadjuvant therapy in patients with muscle-invasive bladder cancer	IND approved by the FDA	asieris.com
ImmunityBio	Anktiva in combination with standard chemotherapy and Trodelvy (sacituzumab govitecan-hziy)	advanced triple-negative breast cancer	IND approved by the FDA	immunitybio.com
Oryzon Therapeutics	vafidemstat	borderline personality disorder	IND approved by the FDA for phase 2b trial	oryzon.com
Xilio Therapeutics	XTX101	solid tumors	IND approved by the FDA	xiliotx.com
Siranomics	STP705	skin squamous-cell carcinoma in situ	IND approved by China's National Medical Product Administration	sirnaomics.com
LivaNova	aura6000 System, implantable hypoglossal neurostimulator	moderate-to-severe obstructive sleep apnea in adults	Investigational Device Exemption approved by the FDA	livanova.com
Quidel	Sofia Q	rapid antigen test device	Emergency Use Authorization granted by the FDA	quidel.com
Blueprint Medicines	Ayvakit (avapritinib)	advanced systemic mastocytosis (SM), including aggressive SM and SM with an associated hematological neoplasmand mast-cell leukemia	approved by the FDA	blueprintmedicines.com
Eton Pharmaceuticals	Rezipres (ephedrine hydrochloride injection)	hypotension occurring in the setting of anesthesia	approved by the FDA	etonpharma.com
Gilead Sciences	Epclusa (sofosbuvir/ velpatasvir)	chronic hepatitis C in children as young as three years regardless of HCV genotype or liver disease severity	approved by the FDA for new formulation	gilead.com
AVITA Medical	Recell System in combination with meshed autografting	treatment of all sizes of acute full-thickness thermal burn wounds for both pediatrics and adults	approved by the FDA for expanded use	avitamedical.com
Neo Medical Osartis	Neo Pedicle Screw System in combination with BonOs Inject cement	compromised bone quality in late-stage tumors	approved by the FDA	neo-medical.com osartis.de/en
Stratatech	StrataGraft	deep partial-thickness burns	approved by the FDA	mallinckrodt.com/stratatech

JobWatch

The Source for Clinical Research Jobs and Career Resources

Twice monthly, *CWWeekly* provides featured listings of clinical research job openings, upcoming industry conferences and educational programs from **JobWatch**, CenterWatch's online recruitment website for both clinical research employers and professionals.

Jobs via Kelly Services

Clinical Research Coordinator
Garden Grove, CA

Biobank Research Scientist
Waltham, MA

Project Manager Lead
Gaithersburg, MD

Regulatory Affairs Specialist
Chaska, MN

Clinical Advisor - NIH
Rockville, MD

Quality Assurance Technician
Irvine, CA

Research and Development Compounder
Pacoima, CA

Research and Development Technician
Hayward, CA

Quality Control Supervisor
Garland, TX

Chemist
Norcross, GA

[VIEW ALL KELLY SERVICES JOBS]

More Jobs

TrialMaster Analyst
Computer Task Group
Work Remotely

IRB Affairs Specialist
WCG IRB
Cary, NC (Remote)

Research Assistant
University of Tennessee Health Science Center
Memphis, TN

Data Coder
WCG KMR Group
Chicago , IL

Manager, Clinical Site Services
WCG ThreeWire
Bloemfontein, South Africa (Remote)

Finance Manager
WCG ACI Clinical
Bala Cynwyd, PA (Remote)

Client Service Manager
WCG Trifecta Clinical
Indianapolis, IN

Institution Partnership Manager
WCG IRB
Puyallup, WA (Remote)

[VIEW ALL JOB LISTINGS]

Upcoming Event Highlights

Webinars

JUNE 24, 2021
Tips for a Successful DMC Organizational Meeting
2:00 PM ET

JULY 13, 2021
Decentralized Clinical Trials: Benefits of a Better Patient Experience
11:00 AM – 12:00 PM EDT

Virtual Conferences/Workshops

SEPT. 28–30, 2021
4th Annual WCG MCC Clinical Trial Risk & Performance Management Collaborative vSummit
9:00 AM – 4:00 PM EDT

OCT. 18–21 & OCT. 25–28, 2021
MAGI's Clinical Research vConference – Fall 2021
11:00 AM – 5:00 PM EDT

On-Demand Webinar

How Can the Accelerated Availability of Pfizer-BioNTech's COVID-19 Vaccine be Replicated?

[VIEW ALL EVENTS]

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