CenterWatch Weekly

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Trial Complexity, Endpoints Continue To Increase, Stretching Site Resources

By Charlie Passut

The average number of trial endpoints has increased by 6 percent on average each year since 2003, leading sites to struggle to meet sponsor deadlines and overwhelmed by the amount of work required to handle such complex trials.

Industry experts say some of the growing complexity and additional endpoints are justified as sponsors adopt trial designs that are more friendly to participants. But such designs often rely on technology that, while easing the burden on participants, also fuels enormous growth in the volume of collected data. Phase 3 protocols now collect an average of 3.6 million data points, three times more than a decade ago, according to a new report by the Tufts Center for the Study of Drug Development (CSDD).

"For sites, the danger is the burden that it places on them, at the same time they're expected to meet pretty aggressive timelines in studies," CSDD Director Ken Getz told *CenterWatch Weekly*. "It's harder to find and retain study volunteers given the eligibility criteria and the demands that are placed on participants in trials, so what this report signals is that even more burden will be placed on those parties that have to administer and participate in a trial."

The CSDD report, based on data from a working group study conducted between February and November 2020, compares trends in endpoints and eligibility criteria

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Return to Focus on Risk Management Postpandemic Could Prove Challenging to Sites

By Charlie Passut

Risk management may be an integral part of conducting a trial, but in the past year sites have been overwhelmed with emergency measures needed to keep their trials running, leaving them little time to attend to the formal processes of identifying, assessing and mitigating risk. As the COVID-19 crisis eases in coming months, however, sites will need to refocus their attention and efforts on their risk management programs.

How they do that will depend largely on the size and experience of their staff.

"I worry that with the events of the last year, some of these risk management plans may have taken a back seat," says Sandra Smith, senior vice president for clinical solutions and strategic partnerships at WCG Clinical. "So now, as people are coming into the normal workflows, they're playing a little bit of catch-up," Smith says.

But catching up with risk management could be difficult for some sites, especially smaller ones, she says. While larger organizations may have personnel they can dedicate to assessing risk and areas of past failures, smaller sites' staff already divide their attention among a variety of trial management tasks. "They just don't have that diversity of resources or the head count," she says, to devote strictly to managing risk.

Jill Heinz, director of clinical research at Injury Care Research, agrees that larger sites have more resources to apply to

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COVID-19 Update

COVID-19 Drug Research Roundup

COVID-19 Vaccines:

Moderna is giving people who participated in its phase 1 vaccine trial the option to receive a third booster shot through a new clinical trial set to begin in July, the company disclosed last week.

The German Centre for Infection Research and **IDT Biologika** say their COVID-19 vaccine candidate failed to demonstrate an expected immune reaction in an early-stage clinical trial. The trial was conducted in Hamburg and enrolled 30 volunteers. Disappointing findings from the trial will likely hold up IDT's plans to seek regulatory approval for the vaccine by the end of this year.

Sinovac's COVID-19 vaccine candidate was reported as 78 percent effective at preventing infection, but recent reports suggest the vaccine carries only a 50.4 percent efficacy rate. The previously reported 78 percent effectiveness rate was announced by the Butantan Institute, the organization responsible for conducting trials on the vaccine in Brazil. The data included cases of mild-to-severe COVID-19 and excluded patients with very mild infections. Once patients with very mild infections were included in the analysis, however, the efficacy rate dropped to 50.4 percent. This updated rate barely exceeds the World Health Organization's 50 percent standard threshold for efficacy.

Findings from a phase 1/2a study show **Johnson & Johnson's** (J&J) single-dose COVID-19 vaccine Ad26.COV2.S produced detectable neutralizing antibodies in healthy adults by day 57. At day 29, the investigators observed neutralizing antibody titers against COVID-19 in more than 90 percent of participants following a single vaccination. Interim results of the early-stage trial show the vaccine, also referred to as JNJ-78436735, was well-tolerated and featured high immunogenicity at 5x1010 viral particles. This dose level was selected for additional investigation in the phase 3 ENSEMBLE trial. Local and systemic reactions occurred either on the day of immunization or the day after but usually resolved within a 24-hour period. J&J plans to file for Emergency Use Authorization for their vaccine pending results of the ENSEMBLE trial.

A phase 1/2 trial evaluating **Valneva's** inactivated whole-virus COVID-19 vaccine candidate VLA2001 plans to use **Oxford Immunotec's** T-SPOT Discovery SARS-CoV-2 test to measure the efficacy of the vaccine in healthy participants.

COVID-19 Therapies:

Studies on the effectiveness of convalescent plasma for treating COVID-19 have yielded conflicting results, with the majority of research pointing to its lack of efficacy in patients with severe disease. A new study from **Imperial College London** found that treatment with convalescent plasma does not reduce the risk of death or minimize the number of days on intensive-care support in patients with severe COVID-19. While the treatment wasn't effective for improving disease-related outcomes in the 912 severely ill participants, it also wasn't harmful. The Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) plans to expand its research into convalescent plasma in 4,000 severely ill patients.

A phase 2 clinical trial from **Celltrion** shows the South Korean company's COVID-19 therapy, Regkirona, was more effective than other antibody treatments developed by **Eli Lilly** and **Regeneron** for treating COVID-19. The trial was conducted across 50 hospitals and included 327 patients with mild and moderate COVID-19. Celltrion plans to study the treatment candidate further in phase 3 trials pending a regulatory approval decision by the nation's Ministry of Food and Drug Safety.

Roche's Actemra and **Sanofi's** and **Regeneron's** Kevzara significantly reduced mortality by 24 percent in patients with COVID-19 who required intensive care, according to findings from an National Institute for Health Research-sponsored study in the UK. The study also found that the IL-6 inhibitors reduced hospital stays by 10 days in patients with COVID-19 who were admitted to intensive care. In contrast with these findings, results from trials in Italy and France found little to no benefit with Roche's drug in patients with moderate-to-severe COVID-19.

DalCor Pharmaceuticals has launched a double-blind, placebo-controlled phase 2 study investigating dalcetrapib as a potential anti-viral COVID-19 treatment. The study's main endpoints, efficacy and safety, will be assessed in three different dalcetrapib dose cohorts compared with placebo in up to 200 adult patients. Treatment will be administered over 10 days. Currently, dalcetrapib is undergoing investigation in a phase 3 cardiovascular trial.

Alexion Pharmaceuticals is pausing enrollment in its phase 3 study examining ravulizumab as a treatment for adults with severe COVID-19. The company is hitting the pause button after the study's independent data monitoring committee found in the interim analysis that the therapy lacked appropriate efficacy when tacked onto best supportive care vs. best supportive care alone.

The first patient with COVID-19-induced chronic fatigue has been dosed with rintatolimod in **AIM ImmunoTech's** active AMP-511 Expanded Access Program. The program plans to enroll up to 100 participants with active chronic fatigue syndrome, including 20 of whom may be "long haulers." Researchers of the study suggest important observations related to the study treatment may be reported in May.

A phase 1/2 study involving 24 patients found that umbilical cord-derived mesenchymal stem cells (UC-MSCs) reduced the risk of death and expedited the time to recovery in patients with severe COVID-19. Patients in this study received UC-MSCs plus

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Industry Briefs

Janet Woodcock in the Running for FDA Chief in Biden Administration

FDA veteran Janet Woodcock has reportedly been short-listed by the incoming Biden administration to serve as the agency's next commissioner and will also likely serve as acting chief until the position is filled.

Woodcock is expected to assume the role of acting FDA commissioner on Jan. 20 after President-elect Biden is inaugurated and current chief Stephen Hahn steps down from the agency.

Woodcock, who took leave from her position as director of the agency's Center for Drug Evaluation and Research (CDER) to serve as the COVID-19 therapeutics adviser to the Trump administration's Operation Warp Speed (OWS) initiative, is now reportedly being considered to lead the agency in a permanent capacity.

The long-time CDER director just last week returned to the FDA as principal medical adviser to Hahn and is now performing her OWS duties in addition to her new advisory role at the agency.

But Woodcock is not the only candidate on the Biden team's short list for FDA commissioner. Joshua Sharfstein is also reportedly in the running for the post. A physician with an extensive public health background, Sharfstein previously served as FDA principal deputy commissioner from 2009 to 2011 and led former President Obama's FDA transition team. He is currently vice dean for public health practice and community engagement at Johns Hopkins Bloomberg School of Public Health.

The Biden transition team did not respond to requests for confirmation of the shortlisted candidates and the FDA declined to comment.

Advocacy Groups Voice Concerns Over Bharat's Vaccine Study

Patient advocacy groups in India are claiming that Bharat Biotech failed to ensure trial participants clearly understood their role in a study of the company's Covaxin COVID-19 vaccine.

The allegations, which were made in an open letter to the Indian government, cite issues in the company's informed consent process and reimbursement program. Allegations from the patient advocacy groups state that the language in the informed consent forms for the vaccine trial was difficult to understand, especially for the mostly illiterate study population.

Given that most trial participants were of low income and at a low education level, the advocacy groups argued that trial participants may not have clearly understood the ethics behind the monetary reimbursement Bharat provided for participation.

Bharat has denied the allegations, noting that it had followed regulatory rules for participants in its phase 3 vaccine trial. Bharat also stated that the reimbursement of $10 to each trial participant was provided for expenses and was approved by all institutional ethics committees at all sites.

This latest controversy involving Bharat's COVID-19 vaccine follows other criticisms of the company, including the fact that the Indian government issued an emergency-use approval for its vaccine before phase 3 trials were completed. Also, Bharat reportedly failed to disclose a viral pneumonitis event in a phase 1 trial of Covaxin. Instead, the adverse event was made public after reports about it leaked to the Indian media in November.

Biogen Study Seeks to Identify Biomarkers Using Apple Wearable Technology

Biogen plans to launch a multi-year, observational trial later this year to monitor data from Apple Watches and iPhones to identify digital biomarkers of mild cognitive impairment.

Researchers have suggested that such biomarkers may be helpful for predicting risk of Alzheimer's disease and other dementias. Ultimately, this may also improve the use of early lifestyle and therapeutic intervention efforts to reduce the progression of cognitive decline.

FDA's 2021 Clinical Trial Regulatory Plan Focuses on Diversity, Complex Design

The FDA's plan for regulating clinical trials in 2021 will focus on increasing participant diversity, encouraging complex and innovative trial designs, and qualifying new drug development tools.

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COVID-19 Update

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heparin and best supportive care. The one-month survival rate in the UC-MSC group was 91 percent compared with 42 percent in the control arm. Also, approximately 80 percent of patients who received UC-MSCs recovered by 30 days vs. 37 percent in the control group.

SaNOtize Research and Development has launched trials in the UK to study whether its SaNOtize Nitric Oxide Nasal Spray is effective against COVID-19. The nasal spray was developed to neutralize and eliminate SARS-CoV-2, the novel coronavirus responsible for COVID-19, in the upper airways and halt its progression to the lungs. Tests at Utah State University's Antiviral Research Institute found the investigational nasal spray was 99.9 percent effective at killing the virus within a two-minute period.

Findings from an interim analysis of a **Kintor Pharmaceutical** trial show that treatment with Proxalutamide in female patients with COVID-19 significantly reduced the need for hospitalization, admission to intensive care, need for mechanical ventilation and death compared with placebo. The trial enrolled 168 women with COVID-19 who were treated with Proxalutamide plus standard care or placebo plus standard of care. The interim analysis included 60 patients in the Proxalutamide group and 35 patients in the placebo arm. Enrollment in the trial is expected to be complete by February, and data collection will conclude by March.

UK drugmaker **Synairgen** has dosed the first patient in a global phase 3 trial evaluating an inhaled formulation of interferon beta-1a, SNG001, for treating hospitalized COVID-19 patients who require supplemental oxygen.

Industry Briefs

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The FDA said it will pursue efforts to advance the use of complex innovative trial designs (CID), including complex adaptive and Bayesian trial designs. The FDA will continue to administer the CID Pilot Meeting Program to help sponsors using complex designs increase their interaction with FDA staff and improve clinical trial efficiency.

Another topic of interest to the FDA is improving the use of agency-endorsed drug development tools, such as biomarkers and clinical outcomes assessment tools.

Read the report at https://bit.ly/2Lr24Db.

Confine or Seclude Participants in Bioequivalence Trials, FDA Guidance Says

Sponsors of generic drug products that need to conduct bioequivalence (BE) trials during the COVID-19 pandemic should develop site-specific plans to either quarantine or separate participants to minimize their exposure to the virus, according to a final guidance released by the FDA last week.

The guidance, intended to be in effect only for the duration of the public health emergency, directs sponsors that want to start or resume BE studies interrupted by the pandemic to use one of two trial models.

The first, a confinement or "bubble" design, confines staff and participants to the trial facility for the duration of the trial. The second nonconfinement, or "ambulatory," design schedules procedures at times and locations so that no two participants come into contact and there is time to clean equipment and facilities between visits.

Comments on the guidance may be submitted at any time.

Read the guidance at https://bit.ly/35JMNnz.

Up and Coming

This feature highlights changes in clinical trial organizations' personnel.

Alterity Therapeutics

Alterity Therapeutics has appointed **David Stamler** to CEO. Formerly, Stamler was Alterity's chief medical officer and senior vice president of clinical development.

Asklepios BioPharmaceutical

Asklepios BioPharmaceutical has appointed **Katherine High** to president of therapeutics. Prior to this appointment, High was a visiting professor at Rockefeller University.

Aviceda Therapeutics

Aviceda Therapeutics has appointed **Mohamed Genead** to CEO, **David Callanan** to chief medical officer, **Derek Kunimoto** to chief operating officer and **Christopher Scott** to chief scientific officer. Genead was formerly the chief medical officer at GenSight Biologics, Callanan is clinical professor at the University of Texas Southwestern Medical School, Kunimoto will continue to serve as managing partner at Retinal Consultants of Arizona and Retinal Research Institute and Scott will continue to serve as director of the Patrick G Johnston Centre for Cancer Research and Cell Biology at Queen's University Belfast.

BioTheryX

Robert Williamson has assumed the CEO position at BioTheryX. Prior to this appointment, Williamson was CEO of PharmAkea and ATXCo.

Blueprint Medicines

Becker Hewes, senior vice president of clinical development at Blueprint Medicines, has been named chief medical officer of the company. Blueprint has also announced that **Andy Boral**, the company's former chief medical officer, will transition to executive vice president of clinical development.

DEINOVE

French biotech DEINOVE has appointed **Alexis Rideau** to CEO. Previously, Rideau was the strategy partnership manager at BIOASTER.

DTx Pharma

DTx Pharma has promoted **Bryan Laffitte** from vice president of biology to chief scientific officer. Prior to joining DTx, Laffitte was vice president of biology at Inception Therapeutics.

Eleusis

Eleusis has named **David Nichols** the director of molecular pharmacology. Nichols will continue to serve in his most recent position as an adjunct professor at the University of North Carolina Chapel Hill.

Elevar Therapeutics

Mark Gelder has been promoted from vice president of medical affairs to chief medical officer at Elevar Therapeutics.

Erasca

Former senior vice president and head of development of Nektar Therapeutics, **Wei Lin**, has been named the newest chief medical officer of Erasca.

Immunovant

Immunovant has appointed **Rita Jain** to the role of chief medical officer. Most recently, Jain was senior vice president and chief medical officer of Akebia Therapeutics.

Innocoll

Louis Pascarella has taken the helm of Innocoll as its newest CEO. Pascarella most recently served as the U.S. head of commercial operations at Novo Nordisk.

Ionis Pharmaceuticals

Eugene Schneider has been named executive vice president and chief clinical development officer of Ionis Pharmaceuticals. Prior to this appointment, Schneider was the head of clinical development at Ionis.

Maruho

Atsushi Sugita has been named president and CEO of Japanese pharmaceutical company Maruho. Most recently, Sugita served as marketing director at Janssen.

Myovant Sciences

Dave Marek has been appointed CEO of Myovant Sciences. Most recently, Marek was the chief commercial officer at Axsome Therapeutics.

Ocular Therapeutix

Michael Goldstein, chief medical officer of Ocular Therapeutix, has been promoted to president of ophthalmology.

Pfizer

Patrick van der Loo has been named by Pfizer as the company's regional president for Africa and the Middle East (AfME) region. Van der Loo was most recently the developed Asia cluster lead and general manager for Pfizer's hospital business unit.

Recursion

Ramona Doyle has been named chief medical officer of digital biology company Recursion. Doyle is the former chief medical officer of Blade Therapeutics.

Synthon

Synthon has named **Anish Mehta** the company's new CEO. Mehta was previously the CEO of Theramex prior to joining Synthon.

Versameb

Versameb has found its newest CEO in **Klaas Zuideveld**, the company's former chief development officer. Also, **Friedrich Metzger** was hired by Versameb to take on the role of chief scientific officer. Previously, Metzger was head of discovery of rare diseases at Roche.

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Trial Complexity

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for phase 2 and 3 trial protocols across three study periods — from 2009 to 2012, from 2013 to 2016 and from 2017 to 2020.

CSDD's data show that not only was the average number of endpoints per trial in the 2017 to 2020 period 27 percent higher than in the period from 2009 to 2012, the trend has escalated in the past three years, with the greatest rate of growth occurring since the 2013 to 2016 period. Since 2013, trial protocols have averaged 20 endpoints, with 1.6 of them on average being primary endpoints, CSDD's data show.

From a sponsor perspective, Kathryn King, senior vice president for clinical development at Aptinyx, says there are often good reasons for increasing numbers of endpoints in clinical trials. "Innovative and exploratory studies — for example, phase 2 studies or studies of novel mechanisms — often require a larger set of endpoints to meet their research objectives," she told *CenterWatch Weekly*. "The focus on patient-centric and quality-of-life data in clinical trials is also a driver for additional and important endpoints in studies."

The mean number of eligibility criteria for phase 1, 2 and 3 trials was 31 per trial for each phase in the period 2013 to 2019.

According to CSDD, the mean number of distinct phase 2 and phase 3 protocol procedures in the 2017 to 2020 period was an increase of 44 percent over the 2009 to 2012 period. In the same timeframe, the number of procedures performed per patient increased 69 percent.

And while each distinct procedure was conducted an average of six times during protocol execution in the 2009 to 2012 period, each distinct procedure in the 2017 to 2020 period was conducted, on average, nearly 7.5 times. The report shows the total average number of procedures supporting phase 3 protocols has increased 6 percent annually since 2003, according to CSDD data.

"It's pretty remarkable how many different sources are now contributing data that have to be curated, compiled and then turned into an analysis data set."

—Tufts Center for the Study of Drug Development Director Ken Getz

CSDD found that a typical phase 1 protocol between 2013 and 2019 was conducted in an average of seven investigative sites based in two countries. Meanwhile, phase 2 and phase 3 protocols — conducted in an average of 34 and 87 investigative sites and six and 14 countries, respectively — screened an average of 12 participants, yielding an average six to seven randomized participants per site.

While technological advances and more participant-centric approaches are gaining traction in the industry, Getz said they won't solve other issues identified in the CSDD report, especially the explosive growth in the volume of collected data. Between 2013 and 2019, phase 3 trials collected 3.6 million data points; phase 2 trials collected 2.2 million; and phase 1 trials collected 724,000.

"A remote or virtual trial introduces other solutions that are now sources for data, and all of that has to be integrated and managed," he said. "Somewhere along that chain of support in executing a protocol will be people who are charged with ensuring the quality and integrity of the data that's gathered." Other risk-based approaches to managing data volume, including augmented analytics and artificial intelligence, could "help manage the volume of data. It's pretty remarkable how many different sources are now contributing data that have to be curated, compiled and then turned into an analysis data set."

King said technology "has made data collection, including data collection directly from patients, easier and faster, and it allows sponsors to collect data outside of clinic visits, opening up new paths for investigation in clinical trials. Broader use of improved technology facilitates collection of additional endpoints, in support of the overall objectives of the study."

The average number of investigative sites conducting phase 2 and phase 3 trials in the 2017 to 2020 period was 33 percent higher than in the 2009 to 2012 period, CSDD says. In the same time period, the mean number of countries where phase 2 and phase 3 trials were conducted nearly doubled.

That increase, CSDD says, leads to more complex trials because of a corresponding increase in events, such as "interactions with additional regulatory agencies and health authorities, delivering trial supplies and monitoring clinical trials in widely dispersed areas."

CSDD attributed the growing complexity of trials to biopharma's "more ambitious and customized drug development activities. Growing investment in treatments targeting rare diseases, efforts to stratify participant subgroups using biomarker and genetic data, and increasing demand for structured and unstructured patient data from numerous sources — encompassing both clinical research data and real-world evidence — are all contributing factors, and they are likely to continue to drive still more complex clinical trials."

Jasmina Jankicevic, vice president for medical affairs at Premier Research, says the complexity of protocols is mostly, but not always, justified. In an era of precision medicine, she says it was necessary

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risk management. "In my experience, the larger sites seem to have this under control a bit better because, as they've grown and have more personnel, they also have the capacity to hire for positions that address this," Heinz told *CenterWatch Weekly*. But small sites have their own advantages when dealing with risk, she says. "Smaller sites have the ability to pivot and adapt quicker when perceived risks are brought to light. So, there is really a benefit to both models."

For smaller sites that don't have the capability to hire someone to conduct risk management, training and assigning the responsibility to a CRC might be enough, Heinz says. "Even if a checklist was created that staff talked through when a new protocol was being initiated, [that] would be a good start. Then, bring that list back out each month or quarter to see if the risks and mitigation techniques are working as planned."

One tool sites can use as a kind of shortcut to identify the risks their trials face, says Laurie Halloran of Halloran Consulting Group, is the report of results from site qualification visits and interviews sponsors conduct when choosing sites to conduct their trials.

Site qualification is "very much a job interview and assessment of the site's people, process and quality," Halloran told *CenterWatch Weekly*. Gaps, weaknesses and areas of doubt discovered by sponsors can be used as an almost ready-made list of risk factors that need to be addressed, she said. "Sites should use the qualification as a way to learn more about what they should do better."

Smith agrees. "Where this becomes incredibly important is when the prestudy visits are done and the sponsors and CROs have essentially been put in the role of assessing the viability of the site," she said. "In essence, what they are doing is looking at what the potential concerns are, what the likelihood is that they are significant or not, and [whether] they could be overcome."

"I worry that with the events of the last year, some of these risk management plans may have taken a back seat."

—Sandra Smith, senior vice president for clinical solutions and strategic partnerships at WCG Clinical

Risks of high severity and likelihood should be eliminated from a trial, while lower-severity risks or those less likely to occur can be mitigated through such measures as liability insurance or the use of a data safety monitoring board. Risks at the lowest end of the scale could just end up being tolerated, Smith says. "This is a hard thing for sites because everyone is an optimist and they think they'll be able to address [a problem]," Smith says.

Rebecca Scott, product support specialist at HealthStream, encourages sites to use a three-pronged risk management approach outlined by the Institute of Internal Auditors' (IIA). According to IIA's Three Lines of Defense Model, sites' risk management programs include:

- Oversight by a governing board, which provides accountability to stakeholders for organizational oversight;
- Actions by management and operational leaders to achieve organizational objectives, including managing risk (first- and second-line roles); and
- Independent assurance through an internal audit (third-line role).

While all of the aforementioned tools "are great and worthy endeavors," Heinz says that in the real world, sites don't use them as often as they could. "When we're scrambling to onboard a study, sometimes they're not practical. We're fighting against quickly getting a study up and running due to sponsor pressures and competitive enrollment as well as ensuring we conduct some of these risk assessments so we can ensure quality data. It's a balancing act."

Smith emphasizes that sites thoroughly document every part of their risk identification, assessment and mitigation strategies in order to protect quality assurance and compliance. Documentation gives a site and regulators the ability to reconstruct a trial as it happened and allows independent observers to confirm the results.

One common mistake among sites, according to Heinz, is calling a halt to their risk management practices once they believe all risk has been fully mitigated. "A site identifies and assesses a potential risk, they take action to mitigate it and then stop there," she says. "Part of risk management is circling back to review if that specific action was effective." She added that sites should ask themselves if they could have done things differently or if their mitigation action caused other issues. "I know I've been guilty of not fully finishing the cycle and have learned that lesson the hard way."

"There is always value for sites to look at both themselves and others," Halloran agrees. "There is no such thing as perfection, every study is its own set of complexities and opportunities for improvement. One big thing is to cultivate a culture of both quality and continuous improvement, encourage project postmortem improvement discussions and a culture of education." Sites that depend on continuing a relationship with sponsors, she says, "do these things and ideally learn from their mistakes."

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for researchers to understand the effect of a medicinal investigational product in different subgroups based on the genetic and cell/tissue/organ levels — where the expression of specific genes and biomarkers are noted, respectively — as well as clinician- and patient-reported outcomes. "The importance of, and demand for, real-world data is another contributing factor," she told *CenterWatch Weekly*.

Jankicevic emphasized that in order for a study to meet strategic goals in development, data quality is of essence. "The proper feasibility assessment of the protocol has to take into account the impact of the protocol complexity on the ability of sites to perform well, with the highest accuracy, reliability and consistency."

"The art of smart protocol design is striking a balance between scientific curiosity and operational feasibility," Jankicevic said. "Protocol amendments are most often a consequence of learnings from sites and patients once the study is initiated. Those are better to be anticipated and prevented by engaging patients, as well as investigators and research site managers, in the protocol development."

But Jankicevic said complex aspects to protocols still need to be done, and comprehensive and ongoing site training plays a key role. "Only well-trained and supported research site teams will be able to generate high-quality study data. Sites are better off being vocal about their protocol-related concerns and then working on developing solutions together with the sponsor."

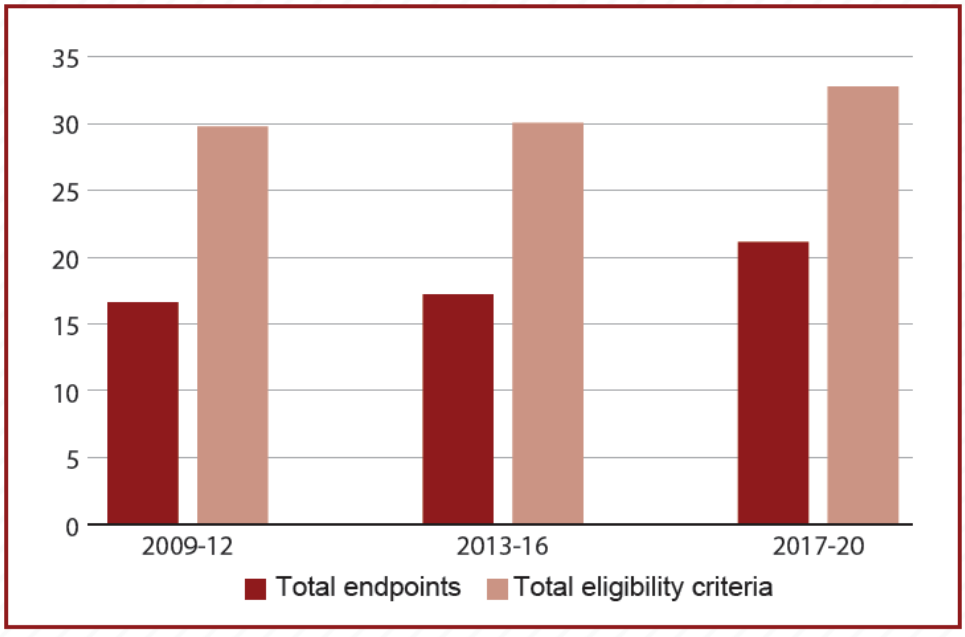
The pressures of conducting trials during a pandemic have prompted discussion of endpoint simplification, Getz said. The pandemic may have helped raise sponsors' sensitivity to focusing on the core objectives and endpoints of a study. He said trials that received input from sources, such as patient advisory boards or advocacy groups, "may be favoring a more relevant design where not only are the number of endpoints perhaps reduced, but the core endpoints, the most clinically meaningful endpoints, have been defined by the patients themselves. That's another way to create focus on core endpoints."

King concurred, adding "the pressure of COVID-19 required sponsors to look carefully at how and where endpoints were collected. For endpoints that are critical to the study objectives, sponsors are now exploring at-home visits by medical personnel, telemedicine visits and procedures that can be completed by patients remotely using technology or sensors."

CSDD said 18 pharma and biotech companies and two major CROs participated in the working group study and submitted data from protocols that were completed, or had achieved database lock, by the end of 2019. A total of 142 data variables from 220 protocols — 60 in phase 1, 85 in phase 2 and 75 in phase 3 — across multiple therapeutic areas, were analyzed by Getz and CSDD's Michael Wilkinson and Zak Smith.

The report is available for purchase from CSDD's website here: https://bit.ly/3igJB8k.

Increase in Number of Endpoints and Eligibility Criteria in Phase 2 and Phase 3 Trials



Note: All values are means.

Source: Tufts Center for the Study of Drug Development

Drug & Device Pipeline News

Company	Drug/Device	Medical Condition	Status	Sponsor Contact
COVID-19 Trials and Actions				
Codagenix Serum Institute of India	COVI-VAC	single-dose, intranasal, live attenuated vaccine against SARS-CoV-2	first patient dosed in phase 1 trial	codagenix.com seruminstitute.com
DalCor Pharmaceuticals	dalcetrapib	oral anti-viral treatment for COVID-19	initiation of phase 2 trial	dalcorpharma.com
Innovation Pharmaceuticals	Brilacidin	hospitalized COVID-19 patients	Fast-Track designation granted by the FDA for phase 2 trial	ipharmInc.com
PerkinElmer	PerkinElmer New Coronavirus Nucleic Acid Detection Kit	testing of individuals without COVID-19 symptoms	Emergency Use Authorization (EUA) granted by the FDA	perkinelmer.com
Quanterix	Simoa SARS-CoV-2 N Protein Antigen Test	detection of SARS-CoV-2 virus nucleocapsid protein	EUA granted by the FDA	quanterix.com
Other Trials and Actions				
Editas Medicine	EDIT-301	sickle cell disease	IND approved by the FDA	editasmedicine.com
Vor Biopharma	VOR33	acute myeloid leukemia	IND approved by the FDA	vorbio.com
Chipscreen Biosciences	chiauranib	second-line treatment of small-cell lung cancer	IND approved by China's National Medical Products Administration (NMPA)	chipscreen.com
Gracell Biotechnologies	GC007g, allogeneic donor-derived anti-CD19 chimeric antigen receptor (CAR)-T cell therapy	B-cell acute lymphoblastic leukemia	IND approved by China's NMPA	gracellbio.com
aTyr Pharma Kyorin Pharma	ATYR1923 (KRP-R120)	interstitial lung disease	completed last subject visit in phase 1 trial	atyrpharma.com kyorin-pharm.co.jp
Jounce Therapeutics	JTX-8064 as a monotherapy and in combination with either JTX-4014 or Keytruda	advanced solid tumors	initiation of phase 1 trial	jouncetx.com
Jupiter Orphan Therapeutics	JOTROL	rare diseases, including ataxias, lysosomal storage disorders and mitochondrial diseases	first patient dosed in phase 1 trial	jupiterorphan.com
OX2 Therapeutics	immunotherapy	recurrent glioblastoma	first patient dosed in phase 1 trial	ox2therapeutics.com
Rezolute	RZ402	diabetic macular edema	initiation of phase 1 trial	rezolutebio.com
Clearside Biomedical	CLS-AX (axitinib injectable suspension)	neovascular age-related macular degeneration (wet AMD)	first patients enrolled in phase 1/2a trial	clearsidebio.com
Felix Biotechnology	YPT-01	chronic P. aeruginosa infections in cystic fibrosis	initiation of phase 1/2 trial	felixbt.com
Terns Pharmaceuticals	TERN-101	nonalcoholic steatohepatitis	patient enrollment complete in phase 2a trial	ternspharma.com

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Company	Drug/Device	Medical Condition	Status	Sponsor Contact
Adverum Biotechnologies	ADVM-022	diabetic macular edema	patient enrollment complete in phase 2 trial	adverum.com
Cytokinetics	CK-274	hypertrophic cardiomyopathy	first patient dosed in cohort 2 of phase 2 trial	cytokinetics.com
Immutep	eftilagimod alpha	head and neck cancer	patient enrollment complete in phase 2 trial	immutep.com
Cara Therapeutics	oral Korsuva (difelikefalin)	moderate-to-severe pruritus in patients suffering from notalgia paresthetica	initiation of phase 2 trial	caratherapeutics.com
OncoSec Medical	TAVO (tavokinogene telseplasmid) plus Opdivo (nivolumab)	neoadjuvant therapy prior to surgery in patients with operable, locally or regionally advanced melanoma	first patient dosed in phase 2 trial	oncosec.com
Redhill Biopharma Cosmo Pharmaceuticals	Rifamycin SV-MMX 600mg	diarrhea-predominant irritable bowel syndrome	completion of phase 2 trial	redhillbio.com cosmopharma.com
REMD Biotherapeutics	volagidemab (REMD-477)	type 1 diabetes	patient enrollment complete in phase 2 trial	remdbio.com
Mirum Pharmaceuticals	volixibat	primary sclerosing cholangitis	first patient enrolled in phase 2b trial	mirumpharma.com
RhoVac	RV001	advanced prostate cancer	first patient enrolled in phase 2b trial	rhovac.com
Kintara Therapeutics	VAL-083	newly diagnosed and recurrent glioblastoma	initiation of patient recruitment in phase 2/3 trial	kintara.com
Prilenia Therapeutics	pridopidine	amyotrophic lateral sclerosis	first patient enrolled in phase 2/3 trial	prilenia.com
Arcutis Biotherapeutics	topical roflumilast cream (ARQ-151)	atopic dermatitis	initiation of two phase 3 trials	arcutis.com
Blue Earth Diagnostics	18F-fluciclovine, a positron emission tomography imaging radiopharmaceutical	detecting recurrent brain metastases	first patient dosed in phase 3 trial	blueearthdiagnostics.com
Denovo Biopharma	DB102 (enzastaurin)	patients with newly diagnosed glioblastoma multiforme	first patient dosed in phase 3 trial	denovobiopharma.com
Organogenesis	ReNu, cryopreserved amniotic suspension allograft	management of symptoms associated with knee osteoarthritis	first patient enrolled in phase 3 trial	organogenesis.com
Pfizer	PF-06939926	ambulatory male patients, ages 4 through 7, with Duchenne muscular dystrophy	first patient dosed in phase 3 trial	pfizer.com
Rockwell Medical Wanbang Biopharmaceuticals	Triferic Dialysate	patients with chronic kidney disease requiring hemodialysis	first patient dosed in phase 3 trial	rockwellmed.com chinawanbang.com
TauRx Pharmaceuticals	hydromethylthionine	mild cognitive impairment and mild-to-moderate Alzheimer's disease	patient enrollment complete in phase 3 trial	taurx.com

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Drug & Device Pipeline News

(continued from page 10)

Company	Drug/Device	Medical Condition	Status	Sponsor Contact
Orchard Therapeutics	OTL-200, ex vivo autologous hematopoietic stem cell gene therapy	early-onset metachromatic leukodystrophy	Regenerative Medicine Advanced Therapy designation granted by the FDA	orchard-tx.com
Gemini Therapeutics	GEM103	age-related macular degeneration	Fast-Track designation granted by the FDA	geminitherapeutics.com
Leading Biosciences	LB1148	postoperative gastrointestinal dysfunction associated with pediatric heart surgery	Fast-Track designation granted by the FDA	leadingbiosciences.com
Merus	Zenocutuzumab	patients with metastatic solid tumors harboring NRG1 gene fusions (NRG1+ cancers) that have progressed on standard-of-care therapy	Fast-Track designation granted by the FDA	merus.nl
Abbott	i-STAT Alinity TBI plasma test	rapid handheld traumatic brain injury blood test	approved by the FDA	abbott.com
ClearMind Biomedical	Axonpen System	illumination and visualization of intracranial tissue and fluids and the controlled aspiration of tissue and/or fluid during surgery	approved by the FDA	cbinsights.com

JobWatch

The Source for Clinical Research Jobs and Career Resources

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Jobs via Kelly Services

Contract In-House CRA
Work Remotely

Cellular Manufacturing Associate
Palo Alto, CA

Clinical Supplies- Operational Planner II
Lansdale, PA

Process Development and Manufacturing
Palo Alto, CA

Analytical Scientist
Rockville, MD

Associate Scientist
Spring House, PA

Lab Technician
Menlo Park, CA

Clinical Safety Physician
Horsham, PA

R&D Lab Manager
Rockville, MD

Laboratory Technician
Carlsbad, CA

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More Jobs

Clinical Science Program Manager
Fanconi Anemia Research Fund
Work Remotely

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University of New Hampshire
Durham, NH

Clinical Specialist - Research & Adjudication
WCG ACI Clinical
Bala Cynwyd, PA

Biostatistician
WCG Statistics Collaborative
Washington, DC

Data Processor
WCG IRB
Puyallup, WA

Clinical Research - Operations Specialist
WCG IRB
Cary, NC

Data Processor
WCG IRB
Cary, NC

Business Development Director
WCG ThreeWire
Work Remotely

[VIEW ALL JOB LISTINGS]

Upcoming Event Highlights

Webinars

JAN. 26, 2021
Reducing Complexity in Starting Clinical Trials: *More Patients, Faster Startup*
1:00 p.m. – 2:00 p.m. EST

JAN. 27, 2021
Medical Device Clinical Trials in China: *Latest Regulatory Developments*
11:00 a.m. – 12:30 p.m. EST

FEB. 11, 2021
Lab X.0: *Addressing Quality and Compliance Challenges in Laboratory Operations in the COVID-19 All-Digital Era*
11:00 a.m. – 12:00 p.m. EST

Virtual Conferences

MARCH 23 & MARCH 25, 2021
Data Integrity for GCP Professionals: *Core Requirements, Expectations and Challenges*
10:00 a.m. – 4:30 p.m. EDT

APRIL 26-29, 2021 & MAY 3-6, 2021
MAGI's Clinical Research vConference
11:00 a.m. – 5:00 p.m. EDT

[VIEW ALL EVENTS]

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