

Clinical Trial Trends & Insights 2024

Intelligently connecting data and insights to navigate the clinical research trends of tomorrow



Advancing health is all about connections. Connecting people, data, insights, and technology for a better, more efficient clinical trial experience. So as the calendar turns over to another year, we've asked our scientific and subject matter experts to connect our data with their expertise and share their thoughts about what trends, changes, and innovations they are looking forward to in 2024 and beyond.

While the industry continues to adjust in a post-COVID world, as of this publication we expect clinical trial starts in 2024 to be up slightly over 2023. Despite this improvement, disconnects remain. Sites continue to struggle with resourcing and the demands of working in multiple technology platforms. Sites, sponsors, and CROs are working to bridge the gap between artificial intelligence, machine learning, drug development, and

decision making. All stakeholders are focusing on the continued promise of digital health tools that provide researchers with real-time data, as well as new approaches to clinical trials that prioritize the needs of participants first — beyond the protocol.

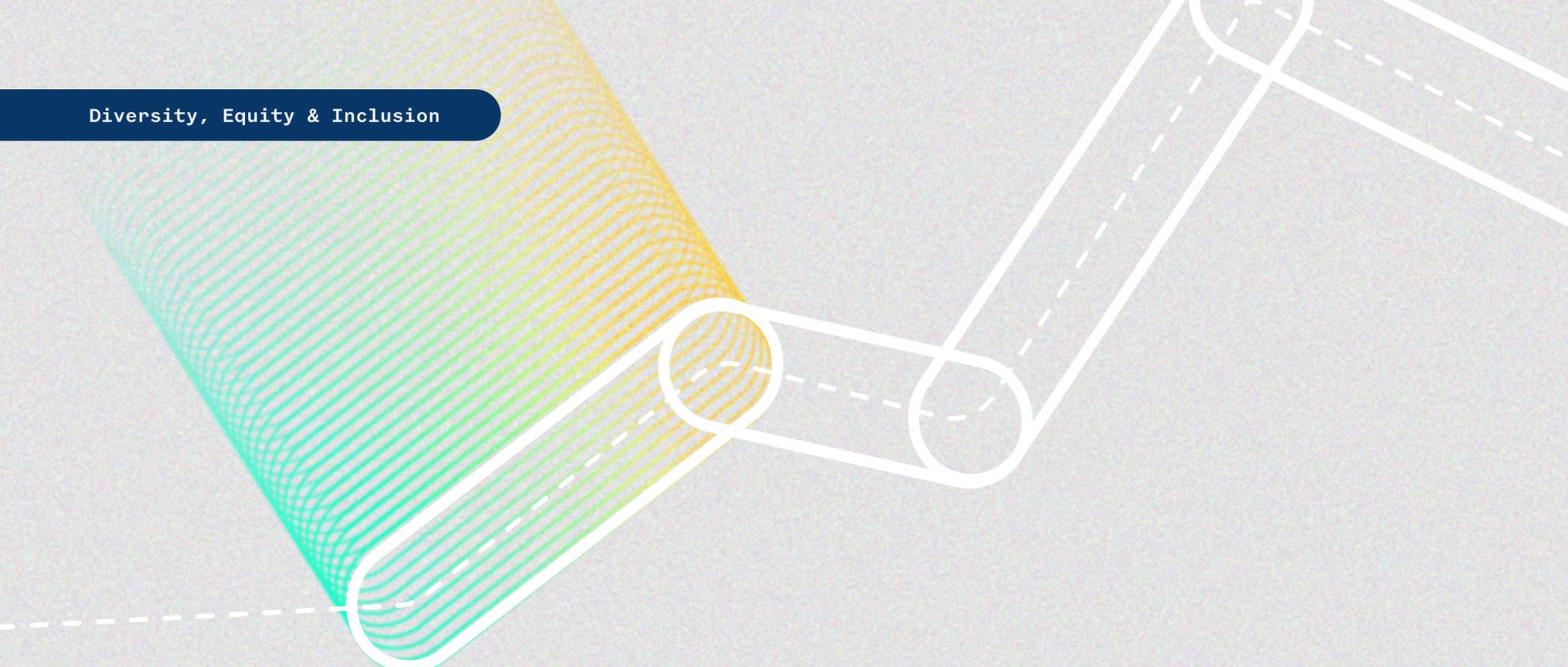
In these pages, our experts will connect you with insights to prepare you for what we expect to be another progressive year in the clinical research industry.

**Diversity, Equity
& Inclusion 4**

**Decentralized &
Hybrid Trials 11**

**Research Site
Readiness 15**

**Emerging
Opportunities 26**



Current Opportunities and Outcomes in Rare Disease Clinical Trials

Lack of diversity in clinical trials can impair quality, increase costs, and put patient safety at risk. Many therapies work differently depending on a person’s gender, race, and ethnicity, so without diverse participants, scientists and clinicians have only a limited understanding of the effectiveness and suitability of treatments for underrepresented populations.

These critical differences are eventually discovered — after the therapeutic has been approved and is in widespread use. The barriers to diversity have been well-documented, but despite significant progress, the industry still struggles to overcome them.

While everyone agrees on the importance of diversity in clinical trials, the 2021 WCG Avoca State of the Industry Report: Diversity in Clinical Research Execution and Participation found that respondents who saw the pursuit of diversity as a scientific or ethical imperative felt more strongly about its importance than those who considered diversity to be important primarily for regulatory or marketing reasons.

The scientific case for diversity is largely settled. What’s left is continuing to make the case with key stakeholders in moving DEI initiatives for clinical trials forward in a meaningful way. In this section, our experts will make the case for the significance of DEI in rare disease clinical trials.

Importance Ratings for Diversity vs. Primary Reasons Diversity was Considered to be Important*					
		Racial/ Ethnic	Gender	Economic	Patient Journey
Primary Reason Diversity is Believed to be Important	Mostly Scientific	4.1 (50)	4.0 (68)	3.4 (20)	4.0 (71)
	Mostly Ethical	3.9 (33)	3.9 (18)	3.1 (47)	3.9 (13)
	Mostly Regulatory	3.9 (11)	3.6 (9)	2.3 (3)	3.5 (6)
	Mostly Marketing	3.0 (1)	-- (0)	2.2 (25)	3.2 (5)

2021 WCG Avoca State of the Industry Report: Diversity in Clinical Research Execution and Participation

Table: Mean (N) importance ratings type diversity – 1 (no importance) to 5 (critically important)

Diversity, Equity & Inclusion



Sharad Adekar
Medical Chair,
IRB Operations
WCG



Scott J. Hunter, PhD
Senior Scientific Expert,
Neurodevelopmental Disorders
and Pediatric Rare Disease
WCG



Steve Smith
President,
Patient Advocacy
WCG



Arare disease affects, by definition, fewer than 200,000 individuals in the United States, and an ultra-rare disease affects many fewer.¹ Altogether, there are more than 10,000 identified rare diseases affecting more than 30 million Americans and their families, with similar numbers in other parts of the world.² Individuals

with rare diseases and their families face significant challenges due to such factors as uncertainty in and availability of a diagnosis and potential treatment options that ultimately affect their medical, psychological, economic, and social health. Considering rare disease prevalence, a lack of diversity, equity, and inclusion (DEI)

considerations in research of these conditions, and practices around treating them leads to diminished opportunity for care and poorer outcomes. These include limited access to diagnosis and care, ongoing clinical trials for a person living with a rare disease, their child or their partner, and the availability of support for their concerns and ongoing needs.

Patients and families from minority groups, and those who come from less economically stable environments often face significant barriers to safe and accessible health care. These can include a lack of supportive resources, such as parental education and awareness of diagnosis and treatment options, or available access to ongoing clinical trials for their conditions. Further impacting access is the historical mistrust toward clinical research studies many minority communities hold, a lack of community representation, and limited engagement with patient advocacy groups that provide supportive guidance and direction. These limitations can readily lead to a delay in diagnosis and access to available treatment options, impacting potential outcomes. A further challenge for many families, both in urban and rural areas, can be more limited access to resources and facilities where diagnosis and intervention take place. Together, these contribute to diminished opportunities for care and

poorer outcomes for diverse communities affected by rare diseases.

When we think about social determinants of health-related access barriers, we must consider factors related to healthcare professional education and knowledge regarding rare diseases. It is the case that many families first rely on available sources of primary care, including family and general practice physicians or nurse practitioners, who may not be as informed about current information regarding rare and ultra-rare diseases. Similarly, primary care practices may not have enough resources or advanced technologies available for faster diagnosis and treatment options.

These challenges can be further complicated for minority and under-resourced communities when awareness of specialty care and the availability of practitioners versed in understanding the diverse needs of affected individuals is more limited.

Importantly, it has been recognized that there is a significant need to provide healthcare professionals and

clinical trial investigators with relevant continuing education and training about the importance of diversity, equity, and inclusion strategies regarding the diagnosis and treatment of individuals with rare diseases. Starting early with medical and health care training, the integration of curricula regarding the social and behavioral determinants of health has begun to contribute to better coordination of elements of care, leading to faster diagnosis and, when available, access to developing and approved treatments. Furthermore, improving resources and availability of specialist care and adding greater diverse community representation, such as connecting with patient advocacy groups, have improved outcomes for minority persons with rare disease and their caregivers.

More specifically, sponsors running clinical trials, including pharmaceutical companies and the individual investigators conducting their studies, have been directed to think more clearly and to state explicitly within their study objectives and design how they will

directly address diversity and equity considerations. Unique in 2024 is the extent to which emerging practices regarding equitable clinical trials have begun to standardize as drug developers and other stakeholders become familiar with the methods of diversification required of them, which will ultimately lead to a required increase in the numbers of diverse participants who are represented in and serve as beneficiaries of treatment research.

During protocol development, sponsors and investigators are also encouraged to carefully assess research methodologies and approaches, research outreach and recruitment methods, and improve the availability of adequate resources to accommodate minority populations for ease of recruitment. Community-based participatory research methods can support this effort, ensuring that individuals from minority communities with rare diseases are included in the design

and implementation of the research from the start, and by identifying and resolving potential clinical biases. Community-based participatory research uses collaborations between research organizations, investigators, and community members throughout all aspects of a research project. This approach is important given its commitment to engaging and representing intersectionally diverse populations affected by rare and more common diseases and fostering greater engagement across minority communities.

Trial diversity and rare disease drug development together will benefit from the growing collaboration by the FDA regarding the necessity for

diverse and equitable representation in clinical trials and biotech companies' increasing familiarity with the resulting best practices in development. Tools to reduce the diagnostic odyssey will continue to reduce the cost and burden of rare diseases, while advocates' work with policymakers will better open access to these tools and strategies.

The new DEPICT Act passed recently by the U.S. Congress requires the FDA to require sponsors to submit Diversity Action Plans with their Phase III or other pivotal trials. The FDA has urged both large pharmaceutical companies and the growing number of smaller biotech drug developers involved in rare disease research to reach out and work with them early in

“Unique in 2024 is the extent to which emerging practices regarding equitable clinical trials have begun to standardize as drug developers and other stakeholders become familiar with the methods of diversification required of them.”

the investigatory process to develop protocols and find solutions to the challenges this new requirement presents. The DEPICT requirement comes at a time when the industry is a few years further down the road from the events of 2020, including the COVID-19 pandemic, which awakened a new, sincere investment in being more inclusive in health care across all stages of development and ultimate treatment, including clinical research. 2024 is a specific year to watch this investment translate directly into best practices.

Additionally, better tools in genomic screening are available now, which help reduce the diagnostic odyssey and connect rare disease patients with new treatment options and early interventions that can save their lives and prevent unnecessary damage from the disease. Policies to open access to these fresh solutions more broadly across diverse affected communities will remain an active focus for rare disease advocates and collaborating policymakers in 2024.



A growing body of evidence shared recently has shown how policies that help families of rare diseases also benefit society. Two studies commissioned by the EveryLife Foundation for Rare Diseases^{3,4} will be used in dialogue with policymakers: one quantifies the cost burdens on families and society of rare diseases, and the other quantifies the avoidable

costs of the diagnostic odyssey. Legislation is in the works to provide access to treatments and diagnostic tools to people regardless of zip code and income level. Watch for legislative efforts to open access to newborn screening, including rapid genome sequencing, genetic counseling, and early intervention services. Small patient populations have always hampered

rare disease research. As we expand our definition of who participates in the research and its benefits, the population sizes grow.

Lastly, and important to how the process regarding greater diversity and equity in clinical research will unfold, the FDA has already issued draft guidance on enhancing the diversity of clinical trial populations, providing recommendations to sponsors to enroll representative numbers of participants from underrepresented racial, ethnic, gender diverse, and economically diverse populations in the United States. This is being further supported by Institutional Review Boards (IRBs) reviewing current research proposals with an eye toward DEI and representative justice. IRBs play a key role in determining the availability of clinical trials for minority populations in rare diseases. One of the criteria for approval is consideration of the equitable selection of research subjects.

As per the Belmont Report, no individual group should be absolutely included or excluded from clinical study without justifiable scientific or ethical reasoning. IRBs can review the submitted justification and study design for scientific and ethical validity,

and ensure adequate safeguards and protections are in place for the study population more broadly. This will lead to both greater recruitment of diverse participants and clearer knowledge regarding potential outcomes.

ADDITIONAL WCG THOUGHT LEADERSHIP



ARTICLE

FDA's Path Toward Diversity in Clinical Trials:
The DEPICT Act and Sponsor Responsibility



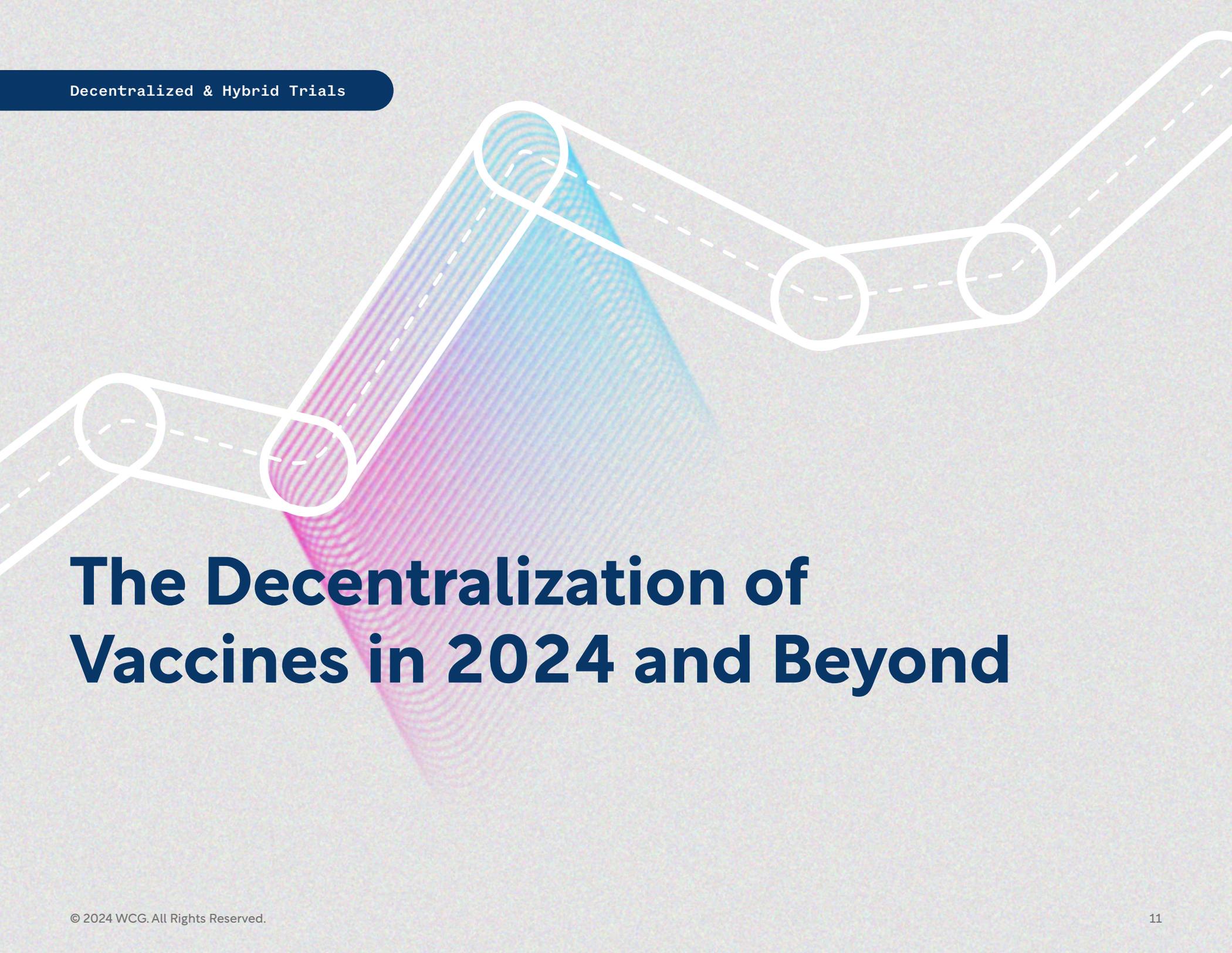
PODCAST

Breaking Down Barriers: How DE&I, Technology,
and Protocol Design Impact Enrollment Success



PODCAST

The Importance of Diversity, Equity, Inclusion,
and Intersectionality in Clinical Research



The Decentralization of Vaccines in 2024 and Beyond

The COVID-19 pandemic drove interest in decentralized (DCT) and hybrid trials. As the world emerges from the global pandemic, the utility of DCT elements continues as DCT and hybrid trials enable the delivery of a more participant-centric approach to research, as treatments can be delivered remotely, sponsors can engage with a more diverse patient population, and recruitment efforts can be accelerated.

But while digital devices, mobile applications, and online communication methods are useful tools, they are not complete solutions. The launch of Apple's ResearchKit facilitated the enrollment of thousands of participants into research programs on a wide variety of chronic diseases, but several weeks later, about 90% of initial enrollees had dropped out of the project. As such, it's important for the industry to determine the right mix of virtual and on-site care.

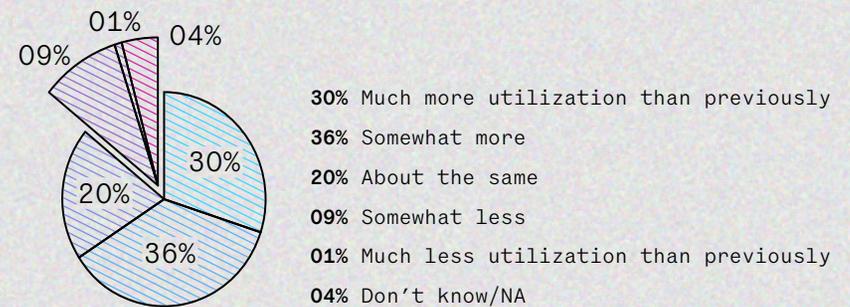
From a regulatory perspective, if the protocol is designed as a DCT or a hybrid trial, some or all research activities may occur at locations that are not traditional clinical trial sites. For example, a local clinic, a mobile unit, or the participant's house may serve as the location for some research activities.

In 2023, the U.S. FDA issued its guidance on the design and implementation of DCTs and updated its position on using electronic systems, records, and signatures in clinical investigations. In addition to guidance development, the

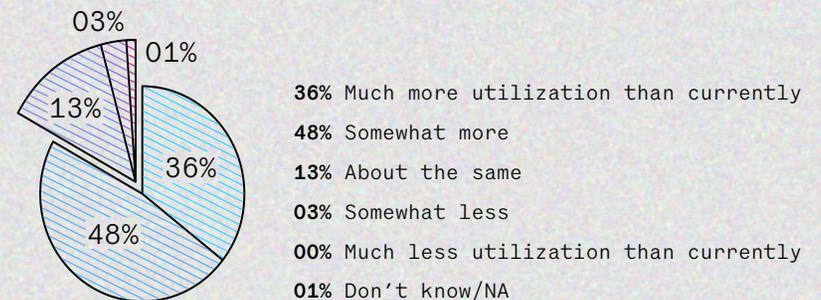
FDA has created a framework that includes workshops, demonstration projects, stakeholder engagement, a website, and internal processes to evaluate DCTs and hybrid trials.

In this section, our expert outlines the impact of DCTs and hybrid trials on vaccines, and how we can continue to bring the promise of more patient-centric care through DCTs.

DCT Adoption 2020-2021*



DCT Adoption 2022



*Clinical Trials Arena DCT Adoption Tracker

According to a *Clinical Trials Arena* analysis, the incorporation of decentralization components in clinical trials was expected to rise by the end of 2023.



Daniel Kavanagh, PhD, RAC
Senior Scientific Advisor,
Gene Therapy, Vaccines,
and Biologics
WCG

Developing protective vaccines for endemic and emerging infectious diseases is a top priority for global health and a promising area for innovation with decentralized clinical trials (DCTs). A DCT is a trial where some or all research activities occur at locations other than a traditional clinical trial site. These activities often include digital screening, remote enrollment, and remote participant monitoring.

The response to the COVID-19 pandemic included the rollout of a variety of innovative hybrid approaches to vaccine trials. As one example, participants were able to collect dried blood spots in the home setting for immune monitoring and to determine the development of vaccine-induced antiviral antibodies.

The potential for remote monitoring for the efficacy of infection and safety events has been clearly demonstrated, and these approaches will play more prominent roles in the coming years.

An emerging area under consideration is direct-to-participant investigational product delivery. With the ongoing development of oral, intranasal, and microneedle array patch vaccine delivery systems, at-home vaccine

self-administration is becoming more plausible. The FDA is currently considering allowing at-home self-administration of an approved intranasal live attenuated influenza vaccine. However, for investigational products, significant concerns related to safety, shipment, stability, privacy, blinding, and compliance create barriers to the rapid adoption of comprehensive direct-to-participant vaccine testing approaches.



Decentralized & Hybrid Trials

Many of the most promising new vaccine technologies involve genetically modified products such as recombinant or synthetic mRNA or DNA, or viral and bacterial vectors. In the U.S., Institutional Biosafety Committees (IBCs) usually oversee the safe handling, administration, and disposal of genetically modified investigational vaccines. IBCs are traditionally based at research institutions and fixed clinical trial sites, and IBC approval requires assessment of facilities, equipment, and procedures at each site.

One solution to the limitations outlined above is the use of mobile research

units. Mobile facilities housed in vans and trailers can bring research capabilities closer to the participants while allowing for careful management of product handling, safety, and privacy concerns. Importantly, with appropriate documentation and advanced planning, mobile research units can be reviewed and approved by an IBC, bringing cutting-edge research to neighborhoods and community settings.

Regarding pandemic preparedness, flexible and adaptable clinical trial platforms will be critical for an agile and timely response to the next emergency. Increasing decentralization of vaccine trials in 2024 and beyond will play a key role in enabling that flexibility.

ADDITIONAL WCG THOUGHT LEADERSHIP



PODCAST

Diversity & Inclusion with Technology in
Decentralized Trials

An abstract graphic featuring a white line path that starts from the left, moves up and right, then down and right, and finally up and right again. The path is composed of solid white lines and dashed white lines. A large, 3D-style cylinder is positioned diagonally across the upper right portion of the image. The cylinder's surface is covered in a dense grid of lines that create a gradient from yellow at the top to red at the bottom. The cylinder appears to be partially wrapped by the white line path.

Supporting Research Sites and the Road Ahead

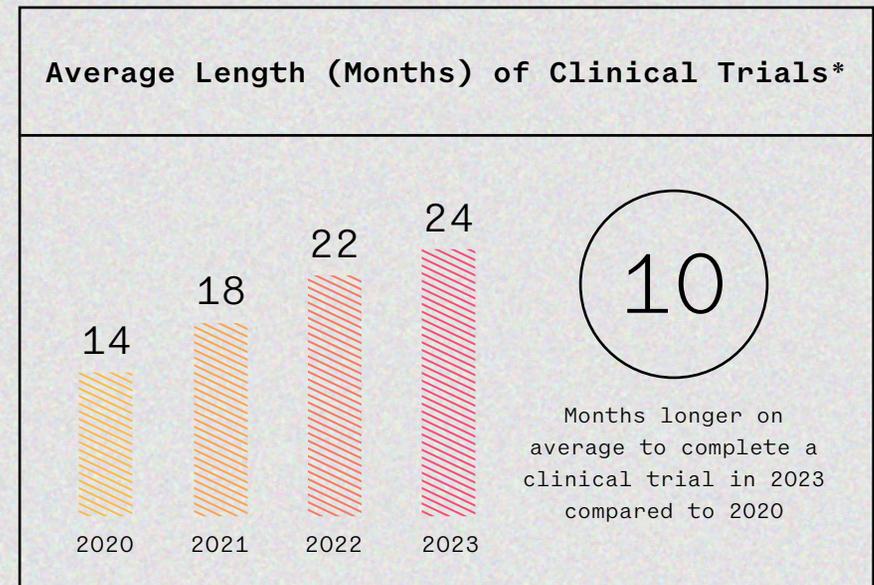
The evolution of clinical research has been dependent on the conversion of Healthcare Organizations (HCOs) to clinical research sites, along with the conversion of Healthcare Providers (HCPs) to Principal Investigators (PIs). These conversions are critical to advancing medicine and providing cutting-edge treatment to patients. However, the current clinical research landscape has become increasingly intricate due to complex protocols, demanding data collection needs, and constricted study timelines, causing a slowdown in the conversion of HCOs and HCPs. As a result, the number of clinical trials now being initiated exceeds the amount of clinical research sites available to conduct these trials.

Because of this, active clinical research sites have become saturated and are facing unrelenting pressure to meet protocol endpoints within the timelines dictated. With only 15% of HCOs conducting clinical research according to industry sources, sponsors and CROs must ensure existing study sites are fully enabled to conduct efficient studies so protocol endpoints can be successfully met. To do this, sponsors and CROs must enable their study sites from the very beginning. Effective site enablement must address

several key factors, including protocol design, training, participant recruitment and enrollment, and more.

Likewise, sites can optimize and grow their research businesses by harnessing solutions that improve site capacity, reduce start-up delays, and lessen their administrative burden. By leveraging site enablement solutions, sites can increase operational efficiency, recruit, and retain more participants sooner, deliver quality data, and improve their financial performance.

Read on for insights into how sponsors and CROs can better enable the research sites conducting their studies and how sites can address site capacity constraints.



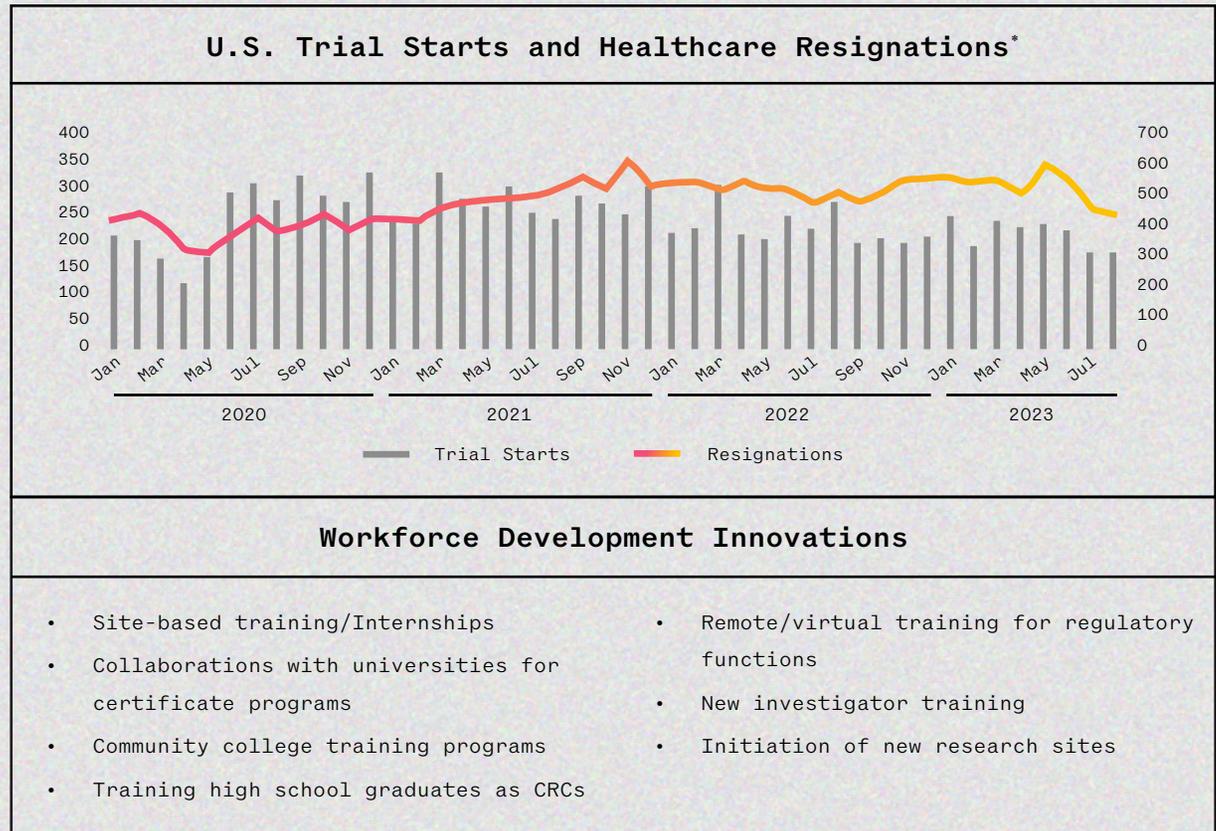
*WCG Data Intelligence & 2022 Tufts Center for the Study of Drug Development

A Look Ahead at Research Sites in 2024



Sandy Smith, RN, MSN, AOCN
Senior Vice President,
Clinical Solutions and
Strategic Partnerships
WCG

The tumultuousness of the ‘pandemic years’ has lessened, giving rise in 2024 to an intense focus on people, timelines, and quality in conducting clinical research. Near the end of 2023, research sites reported more stabilization in the research workforce, consistent with the U.S. Bureau of Labor Statistics report of declining resignations in healthcare (see graphic). Since 2020, the most critical concern at research sites has been workforce retention and recruitment. The availability of qualified research professionals will remain a top concern in 2024. Innovations in



Workforce Development Innovations

- Site-based training/Internships
- Collaborations with universities for certificate programs
- Community college training programs
- Training high school graduates as CRCs
- Remote/virtual training for regulatory functions
- New investigator training
- Initiation of new research sites

*2023 WCG Data Intelligence & 2023 U.S. Bureau of Labor Statistics Report on Declining Healthcare Resignations

workforce development will continue to expand through research sites, professional organizations, and partnerships as the industry highlights the role of the clinical research professional as an intentional career choice (see above).

Aside from workforce issues, clinical trials sites continue to face numerous

headwinds ranging from capacity limitations to increasingly complex protocol designs and the inability to meet trial enrollment targets and timelines. These factors contribute to the increasing trend in clinical trial completion taking an average of ten months longer to complete in 2023 vs. 2020.⁵

While the impact of The Great Resignation has lessened, clinical research sites and pharmaceutical company partners are mutually invested in accelerating clinical trial activation. Focusing on oncology, a therapeutic area representing over 40% of the sponsored trials opened in 2023,⁵ guidance from the National Cancer Institute (NCI) suggests a target activation timeline of 90 days. Some sites report meeting or exceeding this target, but far more are establishing action plans to reduce their activation times currently surpassing 100, 200 or even 300 days.

Across all therapeutic areas, there is disparity in median time for trial activation, defined as time from site selection to completion of contract. For the past 3 years for Phase I-III trials, the median timeframe for Academic Medical Centers (AMCs) and hospitals is 8.12 months vs. independent sites/physician practices with a median of 4.37 months.⁵ With many steps and

variables in the start-up process, one task consuming weeks to months is the negotiation process for both budgets and contracts. Budget negotiation timelines trended an average of eight days longer in 2023,⁵ likely impacted by higher site costs due to inflation. Concentrated efforts on improving activation timelines through workflow optimization will include use of centralized ethical and biosafety review, deployment and linking enabling technologies, evaluating options for outsourcing administrative services, and enhanced communication in negotiations.

“While the impact of The Great Resignation has lessened, clinical research sites and pharmaceutical company partners are mutually invested in accelerating clinical trial activation.”

Recapturing the Progress Made with CTA Negotiations During the Pandemic



Luke Goodpaster
Director, Site Network
WCG



Collin Gruener
Operations Manager,
Site Network
WCG

The time it takes to finalize clinical trial agreements (CTAs) is among the most pressing challenges in clinical trials, but our industry proved during the COVID-19 pandemic that rapid improvement is possible. CTAs that previously took months to negotiate before the onset of the

pandemic were suddenly finalized in a matter of days. However, CTA negotiations have largely reverted to pre-pandemic practices just as research on treatments and vaccines have allowed society to return to some form of normalcy. With trial volume normalizing after a post-pandemic boom and pharmaceutical sponsors and healthcare providers reconsidering their clinical trial portfolios and resources, those involved in clinical trial contracting have an opportunity to refine their processes and standards in a way that would bring us closer to those rapid turnarounds we saw during the pandemic.

We envision stakeholders seeking more opportunities to use a template or another source of agreed-upon

language, including previous CTAs between parties and industry-recognized templates like those from ACTA and MAGI. While some sponsors may, for example, deem ACTA's approach to GDPR or IP ownership insufficient to protect their interests, these types of issues do not preclude the use of templates. It just means some terms, but not all, may require adjustments before final agreement is reached. At the very least these resources can provide a great starting point, allowing the parties to focus on key issues, as was the case when the industry turned to those resources for rapid start-up on COVID-19 trials.

Contract teams also will look for ways to become more efficient in 2024 when templates are not used, and two

“CTA negotiations have largely reverted to pre-pandemic practices just as research on treatments and vaccines have allowed society to return to some form of normalcy.”

ways to improve efficiency are through reprioritization of workload and revising internal standards, such as the CTA playbook. By prioritizing CTAs that are nearly complete ahead of new CTAs, you can shorten negotiation timelines and prevent overaccumulation of contracts on your to-do list. In other words, do not automatically relegate incoming tasks to the bottom of the priority list; focus on reducing the size of your to-do list by resolving those CTAs that can be finalized quickly. Just as we prioritized our vaccine and treatment trials during the pandemic, prioritizing those CTAs that are closest to finalization can have a tremendous effect on turnaround.

Drafting an adaptable CTA playbook that works within a wide variety of CTA templates will help set your contracts team up for efficient CTA negotiations in 2024 and beyond. Focus on key words, phrases, and concepts, with examples of agreeable text to help guide the CTA reviewer. Avoid mandating

“Drafting an adaptable CTA playbook that works within a wide variety of CTA templates will help set your contracts team up for efficient CTA negotiations in 2024 and beyond.”



long blocks of text that are required verbatim. Allowing your contracts team to work key ideas and terms into the existing template language leads to more productive conversations with the opposing side. The first step to accomplishing that goal is strategically drafting or revising your CTA playbook.

Lastly, with efficiency as a priority, teams should be willing to pick up the phone earlier and more frequently. Too often “negotiations” happen in the comment bubbles, especially when the reviewer is short on time. This method, while convenient, is inefficient. It leads to prolonged discussions and more rounds of ineffective back and forth. Simply removing and replacing language with comments such as “not approved” is not negotiation, and it certainly does not constitute collaboration. A phone call allows both parties to clarify points in real-time, which leans more toward collaborative problem-solving than combative dispute.

The decrease in CTA negotiation time that was experienced during the pandemic was more easily obtainable as all parties had the same shared goal of supporting COVID-19 clinical trials. We cannot forget that patients who suffer from any disease or disorder also experience a disruption to their daily lives. While one specific health issue may not have as widespread of an impact as a pandemic, all parties should be able to continue to share this same goal. Focusing on common goals can change negotiations from an adversarial relationship to a team approach. It is important to move away for the “us vs. them” mentality. The clinical research ecosystem requires all parties of a CTA to work together to be successful.

SITE READINESS IN VACCINE TRIALS:

Lessons Learned from the COVID-19 Pandemic



Tyler Bye
Director, Site Solutions
and Product Strategy
WCG

Vaccine research will forever be linked to the COVID-19 pandemic. For all the heartache and troubles the pandemic brought us, it showed the collective power our industry holds when unified for a singular focus. While the pandemic brought new awareness to vaccine research, it also elevated the expectations of sites without accounting for their own aspects of pandemic challenges.

At the height of COVID-19 vaccine research, everyone was on board: site staff, sponsors, CROs, vendors, and most of all, patients, unified for



a singular focus. Our industry, and the world, saw incredible speed and results. Now that the world has progressed and individual factors are no longer aligned, the goal of vaccine research stays the same. Because of this, the next year will see the continued trend of high expectations, with traditional resource constraints

in place, bringing the need to focus on enhancing efficiency at sites.

Sites can maximize resources by leaning into the lessons learned through the pandemic. One practice that enabled the speed of pandemic vaccine research is the clear delegation of duties at sites. Recruitment and retention needs are not mutually

exclusive, but sites should clearly assign the tasks associated across the patient journey to team members. These specific tasks require not just delegation, but dedication from team members. When the team knows who carries each responsibility, members can focus on their specific tasks and work efficiently. The concept sounds simple, but putting it into a repeatable practice takes effort and specialization.

The next year of vaccine development will continue to focus on respiratory diseases, including new variants of influenza and COVID-19.

The year will also see a growing focus on new and emerging diseases such as dengue fever and Zika, and advances in bacterial and viral indications, including meningococcal, hepatitis, and chicken pox. Each specific indication will require sites to focus on healthy but at-risk populations. Sites must continue engaging with the target population to bring awareness of these

vaccine areas and ensure the efficacy endpoints can be achieved.

The industry desires efficiency. Sites can expect sponsors to work on bringing efficiencies through new and consolidated technology. From a site's perspective, some will work, some will not, and the ongoing trend of technical issues will persist. Still, sites should work openly through the challenges and approach changing technologies with the basics of the scientific method. There is a hypothesis that changing technology will benefit research. To continue to advance as an industry, we all need to go through the methodology to determine if the results support the hypothesis.

Vaccine research in 2024 will continue to press forward, and sites will continue to find ways to be more efficient in their processes. The pandemic proved what is achievable, and efficiencies were born from the process. With the mindset of continuous process improvement, patients will be the beneficiaries of the work to come.

Patient Recruitment Barriers in Oncology



Jamie Harper, MHA, CCRP
Vice President, Site Solutions
and Engagement
WCG

As the industry continues to recognize advancements in oncology, it also continues to recognize the challenges in patient recruitment, a vital component in bringing these advancements to market. Patient recruitment comprises two distinct components – identification and enrollment – with each component bringing forth its own set of challenges.

While often overlooked, understanding how patients will enter the study is the first step in developing a successful recruitment strategy to identify potentially eligible patients. The referral pathway can be internal to

the research site through electronic medical records (EMR), through physicians within the same healthcare organization (HCO), or externally through physicians outside the HCO.

Internal referral pathways using EMR are the easiest means to identify potential patients, but it takes time and experience. Building a comprehensive query within the EMR can be challenging due to limitations of the platform and experience of the research staff. Entering complex eligibility criteria commonly found in oncology studies often requires medical record “superusers” to build algorithms for capturing the appropriate patient population. It takes ample resources with the required expertise to properly query the site’s EMR to obtain a list of highly eligible patients for review and potential enrollment.

A properly managed referral pathway continues to the enrollment stage of recruitment. Once highly eligible patients are identified, ensuring they are informed and engaged is critical to successful enrollment and retention. Building a rapport and solid foundation for communication requires patience, understanding, and time. There is a heavy focus on the administrative components of clinical research and the increase in those requirements. The administrative tasks completed in the background are essential to maintaining regulatory compliance but may cause study teams to sacrifice the time needed to build relationships with enrolling patients. Assigning a designated team to address administrative and compliance requirements is impractical for most research sites. Collaborating with a

“While often overlooked, understanding how patients will enter the study is the first step in developing a successful recruitment strategy to identify potentially eligible patients.”

Research Site Readiness

vendor can ensure potential research participants are well-informed and engaged while also supporting administrative and regulatory compliance.

As complex eligibility requirements continue to be a component of clinical

oncology research protocols, developing a strong and comprehensive patient recruitment plan is the first step to mitigating patient identification and enrollment barriers. Utilizing internal resources in combination with the right external partners can help research sites continue the drive forward in conducting clinical research and propel oncology treatments to the next level.

ADDITIONAL WCG THOUGHT LEADERSHIP



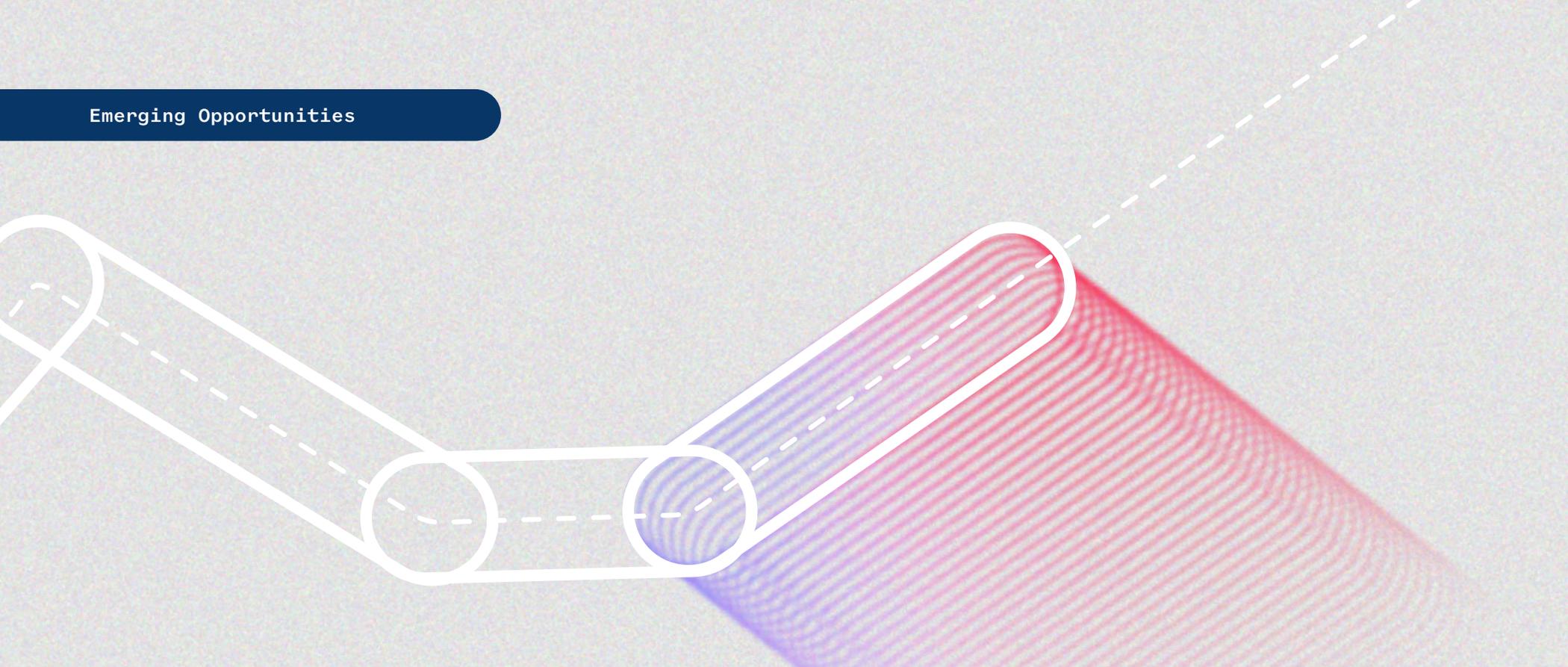
SURVEY REPORT

2023 Clinical Research Site Challenges
Survey Report



PODCAST

Unlocking Site Potential: Reducing Site Burden
and Enhancing Clinical Trial Efficiency

An abstract graphic featuring several overlapping, semi-transparent tubes. One tube is white with a dashed line inside, another is blue with a dashed line, and a third is red with a dashed line. A large, red, semi-transparent cone-like shape is positioned on the right side, overlapping the tubes. The background is a light gray with a subtle grid pattern.

Psychedelics, Artificial Intelligence, and Digital Biomarkers

Artificial Intelligence

The reach and impact of artificial intelligence (AI) throughout the healthcare industry has been steadily growing. From disease diagnosis to the tailoring of treatment plans, AI is starting to appear everywhere. But where is AI's place in clinical trials?

According to the Tufts Center for the Study of Drug Development, a typical Phase III clinical trial generates more than 3.5 million data points. This finding highlights the need for artificial intelligence to manage these massive data sets to deliver insights for better, more timely decision making.

From a regulatory perspective, in 2023 the FDA published a discussion paper outlining the current and future applications of AI and machine learning (ML) in drug development. This paper addressed core issues like human-led governance, data quality, and model development standards. It emphasized a risk-based approach tailored to AI/ML use, emphasizing the importance of accountability and transparency. The FDA is requesting stakeholder feedback to help inform future regulatory activities. It is anticipated that AI will impact all areas of clinical research including protocol development and ethical review of research.

Digital Biomarkers

Digital biomarkers are behavioral and physiological data such as heart rate, physical activity, and step counts collected using digital devices. These measurements can be reflective of treatment response, enabling a better understanding of disease progression, and they have the potential to replace time-consuming assessments that can be difficult for patients.

While this technological shift could introduce risks to clinical trials, it offers long-term benefits to patients and researchers alike when safely developed, assessed, and adopted.

Psychedelics

A recent search of clinicaltrials.gov found nearly 200 clinical trials of psychedelics currently registered. The FDA published its first draft guidance on this topic in 2021, and an expanding body of research suggesting that psychedelics may treat CNS disorders like substance abuse, depression, chronic pain, and schizophrenia has sparked a renewed interest in recent years by drug developers and investors.

This emerging area of research presents exciting opportunities to address important unmet medical needs for many disorders, including CNS. While there are some significant challenges, the potential to make significant strides in improving patients' lives provides a sense of optimism for the future of the field.

On the following pages, our experts will dive deeper into these emerging topic areas of interest.

Past Promises, the Future Hope of Neuroscience Clinical Research



Mark Opler, PhD, MPH
Chief Research Officer,
Clinical Research Solutions
WCG

The past five years have been full of important milestones for neuroscience clinical development, from the approval of the first rapid-acting antidepressant, Janssen's esketamine (Spravato) to the publication of the industry's first late-stage clinical trial of psilocybin by Compass Pathways.⁶ Many of these trends will continue, but they will be accompanied by larger, epoch-scale changes that may permanently alter the way we do research.

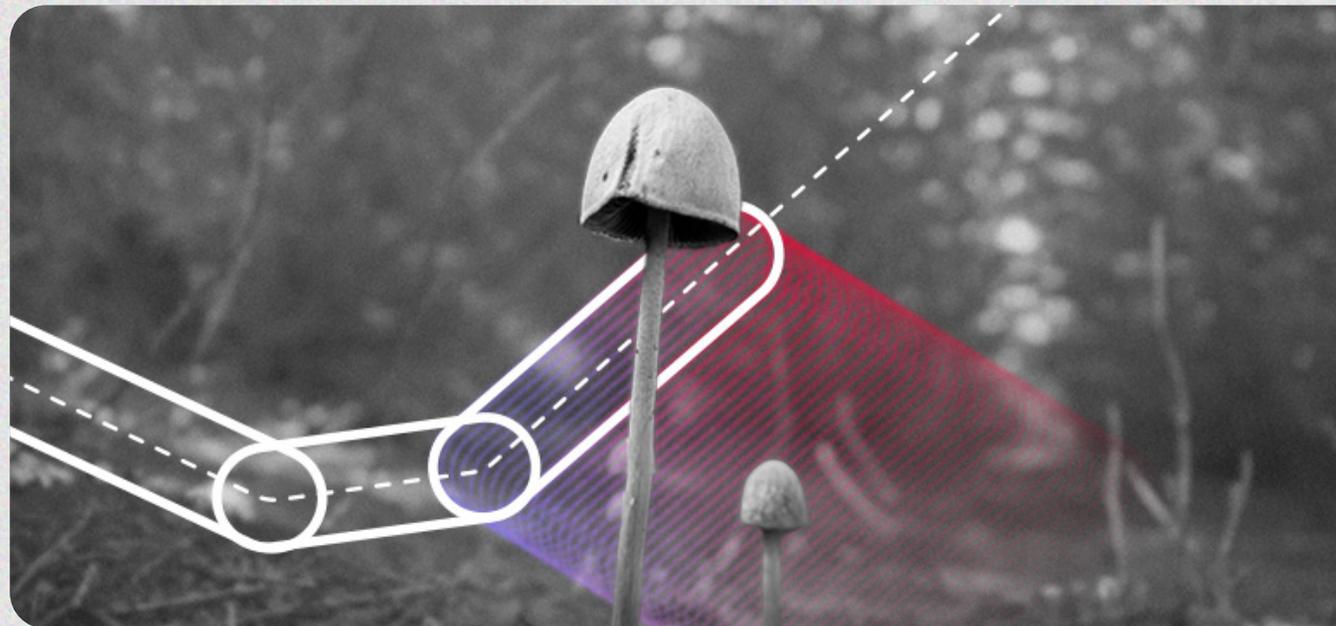
Psychedelics, the most exciting new trend in neuroscience, are not exactly

new – they have been used all over the world for thousands of years, predating the rise of modern industrial medicine. Legal and conceptual frameworks to allow their use in neuroscience research have only recently permitted widespread study, bringing them to the brink of potential approval by the FDA for therapeutic applications.

In parallel with the rise of psychedelics and the continued advances in new treatments for schizophrenia, PTSD, and anxiety disorders, we have seen the evolution of a new area of technologies

collectively referred to as digital biomarkers. The confluence of these two trends, coupled with recent research on novel mechanisms of action, will likely help foster large-scale changes in how neuroscience studies are conducted, particularly in the field of psychiatry.

The central challenges of psychiatry clinical trials have been two-fold: first, the eternal limitations of finding appropriate research participants for disorders that are diagnosed based on subjective criteria and syndromic presentations; and second, the



Emerging Opportunities

difficulty of determining efficacy with measurement tools which require significant training and resources to use correctly, and even in the hands of an expert are often inaccurate and prone to bias.

Rapid-acting antidepressant research has catalyzed a re-examination of study endpoints⁷ and hints at a new method for bridging the gap between objective evaluations, which will enable efficient, sensitive evaluations at scale and the existing validated methods of symptom assessment has emerged in the form of vocal analytics. This field has roots in the 1960s and 70s when researchers used pauses in speech as a measure for neuromotor function.⁸

Recent publications by Johns Hopkins University and others point to the use of simple, valid measures, such as speech latency, as being useful methods for automating objective markers of pathology in depression and bipolar disorder. Future work on this approach



may lead to smaller, more accurate trials that have meaningfully better statistical power (Siegel et al.) and can be conducted more efficiently and ethically.⁹

The next year will bring more reports of continued success with psychedelics and a further crystallization of their unique modality. They may

increasingly come to be appreciated as “synaptogenics,” or compounds that promote the reorganization of the brain, while also demonstrating renewed attention to non-drug therapies as most psychedelics are being packaged with various structured psychotherapies and supportive therapies. An unintended benefit of the psychedelic revolution

might well be the renewed interest in holistic approaches to treatment and a rediscovery of the psychiatric patient as a psychosocial entity, not simply a neurobiological test subject.

Progress is not without its problems. While the past decades have been a time of incredible technological transformation of neuroscience research, the impact on investigative site staff has been challenging. A poster by Cohen et al.¹⁰ shows that the stress of managing technology burdens falls disproportionately on the shoulders of those clinicians assessing patient symptoms. The demand for high-throughput data collection at scale

with strong reliability and accuracy, on top of all the other tasks required by investigators, may finally force the field to consider the limits of this approach.

In conclusion, 2024 may be the year that neuroscience clinical research rediscovers its future in the promises of the past. From the approval of psychedelics known to humanity for thousands of years for their potent neuroactive properties to the renewal of speech analysis as a method of evaluating patient status and the promise of smaller, more humane studies that allow patients and investigators to fully participate in the benefits of our work. With hope and optimism that is hopelessly old-fashioned, we look forward to the coming year.

“2024 may be the year that neuroscience clinical research rediscovers its future in the promises of the past.”

Psychedelics:

From Powerful Potential to the Psychiatrist's Practice



Currien MacDonald, MD, CIP
Medical Chair Director,
IRB Operations
WCG

The list of mental illnesses with high disease burdens and limited effective treatments may be shrinking soon. Psychedelics show great promise in being able to address multiple illnesses plaguing society, and the research investigating this is not fringe science blowing smoke. For example, in 2023 the Office for Human Research Protections held its sixth annual exploratory workshop¹¹ on the ethical and practical considerations of psychedelics research. Also, the FDA granted breakthrough therapy designation in 2017¹² to the

Multidisciplinary Association for Psychedelic Studies (MAPS) for post-traumatic stress disorder, and those active MAPS trials may lead to an approval soon. Moreover, the FDA's first draft, Guidance on Clinical Trials with Psychedelic Drugs,¹³ released in June 2023, shows the way forward for others looking to harness the potential power of these substances and bring them to market.

Truth, it may be a long trip. Psychedelics are still Schedule I drugs, and clinical trials with that class are challenging without other associated issues. While psychedelics may have some utility as just another medicine, their power is likely best

realized in a specific, somewhat unique psychotherapy combination. Research experts in this area, such as those at MAPS and Johns Hopkins University,¹⁴ have amassed substantial experience; however, realizing psychedelics' full potential will take many more extensive trials. Classically trained psychiatrists will need new knowledge, training, and support to conduct these trials. Additional staff—likely also requiring substantial training and support—will be needed to monitor and gather what is often subjective data. Having those tools and being ready for the necessary challenges will ensure that the promise of psychedelics isn't just a pipe dream.

ADDITIONAL WCG THOUGHT LEADERSHIP



PODCAST

Delve into the World of Psychedelic Research and Ethical Inquiry

The Impact of Artificial Intelligence (AI) on Ethical Review by IRBs



Donna Snyder, MD, MBE
Executive Physician,
WCG

The integration of Artificial Intelligence into all aspects of society is moving at lightspeed and is certain to impact the ethical review of clinical research. Currently, there are no federal regulations specific to AI for Institutional Review Boards (IRBs) to follow, but the development of guidance and best practices is likely to evolve over the next few years as IRBs encounter AI applications in all aspects of protocol review. Many research projects that include AI may be exempt from IRB review, either because the study involves secondary use of data without

interaction with a human subject or the data is de-identified.

However, The Secretary's Advisory Committee on Human Research Protections (SACHRP) recently opined on this issue and noted that the "AI/ML [machine learning] and BD [big data] research expose the limits of the traditional concept of identifiability that serves as the basis for privacy protections under the Common Rule."¹⁵ As technology advances, what was considered private in the past may no longer be, so IRBs may need to evaluate the data sources used in research more closely and consider whether adequate protections are in place before establishing that a protocol is exempt from IRB review.

Once a protocol is determined to require IRB review, there are a variety of areas where AI might be incorporated into the research. For example, AI may be incorporated into software as part of a medical device.¹⁶ It may be used as part of drug and biologics development.¹⁷ It could be used to help select what participants

might be enrolled in a clinical trial, or it may be integrated into digital technologies¹⁸ as a study outcome measure.

The IRB is tasked with evaluating how AI will impact the IRB's analysis of benefit and risk, particularly harm related to the validity and bias of models used to train AI¹⁹, as well as how the privacy of the individual will be protected in the research. The IRB is also tasked with ensuring that the informed consent form and process includes information on the use of AI as part of the research if AI is being used to make treatment decisions during the study and is clear on any secondary use of data after the study is complete. IRBs may consider having an individual with expertise in AI/ML available for consultation for complex protocols utilizing AI to ensure that participants are adequately protected.

Deploying AI Across the Clinical Trial Life Cycle



Paul J. Mancinelli, PhD
Chief Technology Officer,
WCG

Artificial Intelligence (AI) techniques across many differentiating industries and domains have grown significantly over the last few years. As in other industries, AI offers great promise across the clinical trial landscape to address common challenges like recruiting and retaining clinical trial participants, identifying the right sites for a particular study, and predicting outcomes to improve the likelihood of a clinical trial's success.

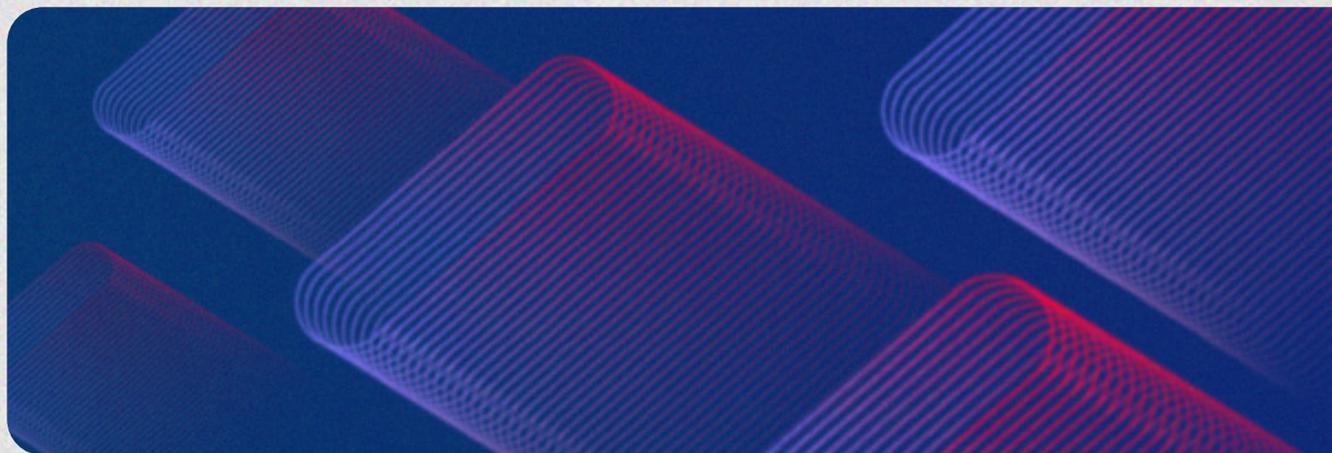
Looking ahead to 2024, technological advancements in AI, particularly with generative AI and Large-Language Models (LLMs), will continue to grow

due to computing availability and the improvement of algorithmic techniques. These advancements in AI, coupled with technology, can address the many challenges and pain points across clinical trials.

According to the National Institutes of Health,²⁰ traditional clinical trial design and execution are time-consuming and inefficient because of many manual processes, leading to only ~10% associated success rate of drugs that receive FDA approval. Given that the drug pipeline has more than 6,000 molecules in clinical development, sponsors require a massive amount of energy, resources, and funds to get these through all phases of trials. The current

technology landscape provides the industry an opportunity to pivot to data and AI-driven solutions that are highly enabled by technology. This means not just digitizing a paper process but reimagining the clinical trial life cycle.

The key challenges in a trial life cycle have remained the same for several years and will only continue to get more intractable if not addressed. Finding and keeping patients, determining optimal sites, data and document management, as well as detecting anomalies in data and the associated time to take corrective actions, will be further exacerbated if the replication of inefficient trial designs continues to reinforce this suboptimal overall process.



Several critical areas of the clinical trial lifecycle exist where AI solutions, including Machine Learning (ML) and LLMs, can alleviate these challenges. Within design and start-up, there is a massive opportunity to use components of AI during document creation and management, such as document review, trial and protocol design, consent, contracts, and study review. LLMs trained on historical documents, combined with indexing, can generate optimal index search criteria, creating a powerful tool to generate documents efficiently and find information quickly. These techniques offer massive time savings in document management and locating key data points and elements within documents. True intelligent automation or augmented intelligence, through the application of effective AI techniques, makes staff more efficient and effective, offering significant improvements in efficiency across an entire organization.

Traditional ML algorithms can be used for site feasibility, site identification, and patient recruitment. In a broader sense, when given a trial protocol, plus historical trial and site performance data, one can determine the optimal set of sites and patients for a given trial. Using ML to identify sites and optimize the identification of patients, there is a ~70% improvement in average response rates from sites willing and able to join trials versus an industry average of 30-50%. By implementing ML techniques, studies have also seen patient recruitment accelerated by ~44%.

In the area of evidence generation, such as electronic Clinical Outcome Assessment (eCOA) and electronic Patient-Reported Outcome (ePRO), monitoring for and detecting anomalies

is crucial for keeping a clinical trial on track with a higher likelihood for success. Applying ML to eCOA and ePRO data in real-time as it is flowing in allows anomalies to be detected and addressed quickly and efficiently. With these techniques, clinical endpoints have a 65% reduction in error rates, drastically improving the likelihood of a trial's success.

Through the use of AI — from ML to generative AI — clinical trials can run more effectively, efficiently, and with higher quality. The application of AI to well-known challenges in clinical trials will alleviate the issues to a great degree in the year ahead and bring life-saving drugs and therapies to society more quickly, ultimately saving lives.

“Using Machine Learning to identify sites and optimize the identification of patients, there is a ~70% improvement in average response rates from sites willing and able to join trials versus an industry average of 30-50%.”

References

1. Bainbridge, M.N. (2020). Determining the incidence of rare disease. *Human Genetics*, 139, 569-574. DOI: 10.1007/s00439-020-02135-5.
2. Smith, C.I.E., Bergman, P., & Hagey, D.W. (2022). Estimating the number of diseases – the concept of rare, ultra-rare, and hyper-rare. *iScience*, 25, 104698. DOI: 10.1016/i.isci.2022.104698.
3. The national economic burden of rare disease in the United States in 2019.
4. The Cost of Delayed Diagnosis in Rare Disease - a Health Economic Study.
5. WCG Data Intelligence, 2023.
6. Goodwin et al, "Single Dose Psylocibin for a Treatment-Resistant Episode of Major Depression" *New England Journal of Medicine*, November 3, 2022.
7. Yavorsky et al, "Recommendations for Selection and Adaptation of Rating Scales for Clinical Studies of Rapid-Acting Anti-Depressants," *Front Psychiatry*, June 2023.
8. E. Szabadi et al, "Elongation of Pause Time in Speech: A Simple, Objective Measure of Motor Retardation in Depression," Cambridge University Press, January 2018.
9. Cohen et al, "Measuring Depression Using an Automated Natural Speech Analysis Pipeline: A Potential Clinical Trial Enrichment Tool," Poster Presented at the 2022 ISCTM Meeting.
10. Cohen, E. A., Montero, J., Grindell, V. M., Wyka, K., Hassman, H. H., Walling, D. P., Blanchard, C. L., Opler, M. G., Michoulon, D., and Ereshefsky, L. (November, 2023). Global raters' work stress and task burnout: An empirical exploration of our primary endpoint evaluators. Poster presented at the Annual CNS Summit Scientific Meeting, Boston, MA.
11. Department of Health and Human Services, Office for Human Research Protections, 2023 OHRP Exploratory Workshop, "Exploring the Ethical & Practical Considerations of Psychedelics Research," September 2023.
12. Multidisciplinary Association for Psychedelic Studies, "FDA Grants Breakthrough Therapy Designation for MDMA-Assisted Therapy for PTSD, Agrees on Special Protocol Assessment for Phase 3 Trials".
13. U.S. Food and Drug Administration, "FDA Issues First Draft Guidance on Clinical Trials With Psychedelic Drugs," June 23, 2023.
14. Johns Hopkins Medicine, Psychedelic Research and Psylocybin Therapy.
15. U.S. Department of Health and Human Services, Office for Human Research Protections, SACHRP Committee Recommendations.
16. U.S. Food and Drug Administration, Medical Device, Digital Health Center of Excellence.
17. U.S. Food and Drug Administration, Artificial Intelligence and Machine Learning in Drug Development, May 2023.
18. U.S. Food and Drug Administration, Digital Health Technologies for Drug Development, December 2023.
19. Cristos Andreas Makridis et al, "Informing the ethical review of human research subjects utilizing artificial intelligence," *Frontiers*, September 2023.
20. Duxin Sun et al, "Why 90% of drug development fails and how to improve it?," *Science Direct*, February 2022.



WCG is a global leader of solutions that measurably improve and accelerate clinical research. Biopharmaceutical and medical device companies, contract research organizations (CROs), research institutions, and sites partner with us for our unmatched expertise, data intelligence, and purpose-built technology to make informed decisions and optimize study outcomes, while maintaining the highest standards of human participant protection. WCG raises the bar by pioneering new concepts, reimagining processes, fostering compliance and safety, and empowering those who perform clinical trials to accelerate the delivery of medical therapies and devices that improve lives. For more information, please visit wcgclinical.com or follow us on X @WCGClinical or LinkedIn.

wcgclinical.com