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Navigating the Changing Clinical Trial Landscape

Perspective from the Field

The only way to map a course to a better future is to understand the reality of the current landscape and what perpetuates the status quo. To do this, insight was gathered from those involved in clinical trials. The output of this research reveals the challenges and priorities that will shape the journey to the future of clinical research.

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Introduction to the Journey

In February 2019, Kathy Vandebelt joined Oracle Health Sciences as Global Head of Clinical Innovation, bringing over 30 years of clinical research and field perspective to the table.

In this role, Kathy helps inform the product strategy to ensure solutions are aligned to deliver the most benefit to site staff and patients, and the most value to sponsors.

Building upon her own experience in the industry, Kathy gathered feedback from the field – study team members, site staff and patients – as well as validated industry trends with biopharma executives, through both primary and secondary research over the course of 2019.

What Kathy learned validated some positions, challenged others and introduced entirely new angles previously unknown. This years' worth of work gathering, synthesizing and understanding the real challenges, opportunities and trends shaping the clinical trial environment is captured in this report. It is being shared in the spirit of "knowledge is power" – the more we, as a holistic community, understand the reality of the field in which we work, the better we can evolve to support and advance the pace of clinical research.

"I really wanted to hone my understanding of the issues and barriers preventing clinical research from being more efficient and effective. To do this, I needed to get out in the field."

KATHY VANDEBELT
GLOBAL VP, CLINICAL INNOVATION

Challenges in the Field

When considering the clinical research ecosystem and understanding key challenges in the space, the perspectives of three core groups were explored – study team members, site staff and patients.

Study Team Perspective

The study team represents the staff designing, conducting and reporting on the clinical trial. The employees may reside at a sponsor or a Contract Research Organization (CRO).

In gathering study team perspective on the current state of clinical research, three themes around the design of clinical trials emerged:

- Performing science in the real world
- Performing adaptive and platform trials set up around a disease versus a drug
- Executing hybrid site models and multiple data collection channels

In discussing these new models, skeptics doubt the desire and willingness of staff to expand the use of decentralized data collection and the likelihood of staff moving away from traditional, centralized, investigator-driven data collection. The desire to "keep the status quo" among study team members, as it relates to trial design, appeared to be tied to self-preservation. The resistance was very real, and the motivation was strong.

In conversations with study teams, keeping the status quo was usually justified by claiming that regulations are the barrier to adopting these new models; however, sometimes this position was due to a lack of understanding. What may appear as self-preservation and resistance to change may be simply a lack of courage to ask or a lack of time to learn.

Despite this resistance to change, there is great support among study team members for improving capabilities within a given work stream, as long as they do not result in a significant change to the function itself. Simply stated, there is an openness to changing the "how" but not the "what."

An interesting point of agreement that was uncovered through conversations was that when a new technology becomes available, sponsors turn to CROs to try it out first. The sponsor looks to the CRO to deal with the challenges of the new solution to assess the feasibility and benefit of adoption. Inevitably, this dynamic is believed to delay the adoption of new technologies by sponsors, as the experiences do not reside at the sponsor to support implementation.

Two other challenges that emerged through conversations and vary across study team members were:

- Talent
- CRO engagements

Situations differed across organizations as to where talent resides, and opinions differed around whether there is a shortage of talent or not. As clinical research becomes more digital and data becomes more accessible, individuals with a deeper understanding of analytics are in high demand. While these skills were isolated to specific functions in the past, they are now more broadly in demand, and there is the expectation that people invest in obtaining these skills.

Outsourcing strategies and the reliance on CROs vary greatly across the industry. A trend at some larger pharmaceutical companies is bringing work that previously was outsourced to a CRO back in house. Opinions differed as to whether CRO engagement created issues or improved performance.

Investigator Site Perspective

The investigator site represents the healthcare professionals who work at the clinical research site, execute the clinical trial protocol and care for the qualified participants who enroll in the trial. Typically, the principal investigator speaks on behalf of the research site community and is ultimately responsible for the conduct of the trial at the site; however, the study coordinator performs the majority of the work. For this reason, it is important to understand the key issues specifically faced by study coordinators, to understand where the operational pain lies.

When asked about the top challenges investigator sites face today, the first three challenges all related to support from the sponsor or CRO in conducting clinical research.

INVESTIGATOR SITE PERSPECTIVE

Challenges faced by investigator sites:

- Budgeting and contract delays
- Support for research-naïve sites
- Lack of efficient data collection models
- Low to negative profitability

From a budgeting and contracting perspective, this is a hot topic fraught with frustration. The source of the pain lies primarily in time delays. Investigator sites feel that the overall budget and contract process takes too long; the time it takes to get a response from a sponsor or CRO regarding a budget submission (average of 30 days) is lengthy, and general cycle times are drawn out to the point of being unacceptable. Adding to the frustration, study coordinators indicated that the overall lags in progress are interpreted as site performance issues by the sponsor or CROs, and that the sponsors and CROs do not acknowledge their role and contribution to delays.

As it related to support for research-naïve sites, which accounts for nearly a third of all sites in a typical study, investigator sites agreed that there is not enough support for those new to clinical research. Medical education and clinic experience alone do not prepare a clinician for conducting research, as different knowledge and skills are needed. Research (testing) and care delivery (treating) are performed differently in a clinical trial setting, and it is important that the site staff understand the laws and framework in which trials operate. To perform clinical research efficiently and effectively, site staff need a comprehensive understanding of the basics. And, increasingly, clinical research requires a solid understanding of emerging and mainstream capabilities and models such as patient-facing technologies, digital endpoints, adaptive designs and basket trials, to name a few. As in medicine, clinical research requires continuing education to ensure investigator site staff are trained and up-to-speed on the latest requirements, techniques and approaches. The feedback from the field, at the site level, is that this initial and continuous education to support participation in clinical research is painfully lacking.

Finally, as it relates to site support for participating in clinical trials, study coordinators agreed that the current data collection systems in place actually decrease productivity instead of increasing it. The execution models to identify study participants and collect the data are burdensome because the systems do not fit easily into the research site workflow and often are not integrated with other systems required to run the trial. Further complicating matters is the fact that, increasingly, data collection is shifting to being collected directly from the trial participant. Study coordinators wish that sponsors and CROs would take the time to better understand how a site operates, and implement data collection methods and systems that make it easier to participate in research, instead of harder.

The last challenge cited by investigator sites relates to the profitability of participating in clinical research. When it comes to enrollment, the complexity of current protocols was cited as a key reason for the drop in site and patient participation. The number of participants an investigator or a site director predicts to enroll in a trial is 25-50% less what they may have predicted a few years ago, due to this increase in protocol complexity. The experienced research staff are finding the potential population does not qualify, or, qualified patients do not want to participate for a variety of reasons including time commitment, convenience, and the sense of invasiveness, just to name a few. Additionally, there is a lack of understanding among site staff around the number of patients needed to breakeven, let alone make participation in clinical research profitable. Study coordinators mentioned that this is also tied to a lack of the Key Performance Indicators (KPIs) they should track to gauge progress to breakeven.

Patient Perspective

Patients represent those people who have the indication of interest of a clinical trial, meet the protocol criteria and may decide to participate in the trial.

For this report, patient perspective was gathered indirectly from study team members and investigative site staff who have direct experience with patients in clinical trials.

Two patient issues emphasized relate to patient recruitment – awareness of clinical trials and engagement in underserved communities.

The overwhelming primary issue reported was the lack of awareness among patients about clinical trials. Not only are they often unfamiliar with what clinical research is, but they also don't realize that there may be clinical trials that could benefit them. The belief is that this is an education issue and/or a health literacy issue, and that special effort needs to be made to ensure outreach into underserved communities.

The other themes regarding patient challenges centered on communication and providing an open feedback loop between the patients and the investigator site and study team. Patients want support for tasks related to participation in a clinical trial and capturing information outside of their daily routine. Additionally, they want to have the ability to provide feedback to help improve and inform the clinical research process along the way. Many sponsors and CROs have committed to supporting this; however, finding a practical and efficient way to do this has been a challenge. Finally, patients want to be treated as humans – not "subjects" – they want to be appreciated and acknowledged during and after the trial.

PATIENT PERSPECTIVE

Challenges faced by patients:
- Awareness of clinical trials
- Outreach in underserved communities
- Communication and an open feedback loop

PATIENTS IN CLINICAL TRIALS

By the numbers:
- **50miles** is the average distance a patient lives from the nearest site
- **<5%** of patients participate in clinical research
- **49%** of patients drop out before study completion
- **48%** of trial sites miss enrollment completion

SOURCE: PharmaVoice Magazine, Nov/Dec 2019, Page 45

Assessing the Landscape

To assess the clinical trial landscape, conversations with biopharma leaders were conducted to get their perspective on trends in the industry.

While recent research found that 60% of trials have protocol amendments during the trial, conversations with biopharma executives suggest this number is low. Also, it is worth noting that protocol amendments are not actually seen as a bad thing; rather, they are seen as a natural part of the research process. That is not to say there is support for poorly defined research nor insufficient attention to details; but rather, it is an acknowledgement of the increase in adaptive design, seamless development from one phase to another and the expected pivots that come with the scientific method.

With regard to reports that 70% of trials run more than one month behind schedule and 85% of trials fail to meet their endpoints, conversations with biopharma executives suggest that the reality is better – these companies are performing better than these averages. Sponsors and CROs are motivated to remain competitive by continuing to improve these metrics now and in the future.

As it relates to reports around manual processes and the intent to leverage digital technologies in clinical trials, this was validated through conversations with biopharma executives. The three greatest opportunities cited during these discussions were:

1. Automating manual processes (e.g. site selection and data collection)
2. Exiting the piloting phase to embrace new ways of working that add value
3. Promote the use of central IRBs

While there are plenty of areas for improvement in clinical trial design and management, there is clear commitment from the biopharma leadership community to make changes to overcome the obstacles in the above listed areas.

CLINICAL TRIALS

By the numbers:

- **60%** of trials have protocol amendments during the trial
- **70%** of trials run more than one month behind schedule
- **85%** of trials fail to meet their endpoints
- **90%** of companies still use manual processes for clinical trial design
- **97%** of biopharma executives intend to leverage digital technologies in clinical trials over the next five years

SOURCE: Everest Group, 2018

Navigating the Path

Based on the complex challenges faced in the field by study teams, investigator sites and patients, coupled with the reality of the clinical trial landscape from the biopharma executive point of view, navigating the path to the future is a bit overwhelming. How do you define it? It starts with identifying those issues that are worth fixing and prioritizing the work needed to address them.

Based on conversations with biopharma executives, this is the priority list of issues:

- Complex "unrecruitable" protocols
- Low awareness of clinical research care options among patients
- Resistance to adoption and a lack of support to help investigator sites evolve to a digital clinical environment

Or stated problems to solve:

- How can we confirm we create manageable, "recruitable" protocols?
- How do we increase awareness of clinical research in healthcare to inform patients of the possibility of clinical trials and facilitate enrollment?
- How do we increase digital competence in the investigator site community and decrease process burden to make a positive difference across the ecosystem?
- How do we create incentives and/or influence regulatory guidance to drive digital transformation and technology adoption to improve the way work is done?

If we are able to map out the course to solving these problems, we can clear the path for smarter, more efficient clinical trials.

Moving Forward

Charting a new path is never easy. For centuries the only way European ships could get to Eastern Asia was sailing around South America. But in the first half of the 16th century, King Charles I of Spain wondered, "could we create a passage through the isthmus of Panama to connect the Atlantic and Pacific Oceans?" While it would take over three more centuries to make that dream a reality, it happened.

We are at a similar point in clinical research. We know there is a better path – we just need to figure out how to make it happen. Unlike dreams of the Panama Canal in the 16th century, we are in a place in history where the technology, the science and the innovation exist to make our dreams a reality.

If we, as a holistic clinical research community, can commit to working together to understand and solve the top challenges in clinical operations, we can remove barriers that are slowing down our ability to bring new drugs to market as quickly as possible to patients waiting in need.

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