CLINICAL OPERATIONS

Insights from the Industry

PROVENTA
INTERNATIONAL

Introduction

Clinical Operations emerge from the pandemic as a truly transformed field. COVID has propelled decentralization of clinical trials, putting the adoption of virtual technologies and the prioritization of patient centricity in the forefront of all endeavors to investigate novel therapeutics. While parts of the industry embrace this newfound world, others remain more reluctant - our Strategy Meetings in San Francisco, Boston and London aim to facilitate discussion on whether these technologies are appropriate for everyone, and how challenges in adopting and implementing them can be overcome. Additionally, as the field moves towards examining new treatment modalities, we discuss the importance of clinical data and how that can be handled better, particularly as we see advancements in the spaces of AI and Real World Evidence. The need to manage more complex biomarkers better also necessitates novel approaches. As we also examine pioneering investigative products, the need for innovative trial designs becomes more apparent. These and other issues were tackled in our Strategy Meetings, as detailed in this report - which we hope you will enjoy reading.

The Editorial Team
Proventa International

TABLE OF Contents

TOP 10 Challenges 2022: What Peers are Focusing on

1 Decentralized Clinical Trials

The increasing adoption of Decentralized Clinical Trials (DCTs) has permanently transformed the clinical operations landscape, with increased focus on patient engagement, diversity and providing resilience to clinical trial protocols in the face of emergent situations such as the pandemic. Delegates seek to navigate the best path forward, adapting DCTs and their elements to their own needs.

2 Supply Chain

Supply chain disruptions were particularly impactful during the pandemic, and much of the industry seeks to future-proof their own manufacturing and logistics solutions. This is particularly pertinent when it comes to clinical trial supply chains, which often come with stringent requirements. Additionally, adapting supply chains for direct-to-patient designs and integrating DCTs to the model comes with its own challenges, which peers seek to resolve.

3 Risk-Based Quality Monitoring

Risk-Based Quality Monitoring (RBQM) provides additional flexibility and resilience, and is proving to be an essential component of clinical trials with complex design protocols, vast data volumes from diverse data sources, and novel supply chains. Delegates seek solutions that can provide failsafes and address quality issues in a timely manner, before such challenges escalate to actual liability.

4 Patient Recruitment and Centricity

Another of the areas highly impacted by the COVID-19 pandemic, trial sponsors now place increasing value in recruiting and retaining patients - many of which are now more reluctant to travel to participate in investigations. Delegates cite the need to build trust and appreciation with patients, often likening clinical investigations as a partnership with patients in today's clinical operations.

5 Study Protocol Design

With an increasing plethora of novel treatments emerging into the pharmaceutical mainstream, delegates seek to navigate the landscape of protocol designs that can accommodate not only such novel therapeutics, but also save time and resources. Many hope for regulatory cooperation in innovative new designs.

TOP 10 Challenges 2022: What Peers are Focusing on

6 Diversity and Inclusion

Medicine should be for everyone, and trials should reflect the maximum market size - not the few who have access to entrenched institutions that often refer patients to trials. DCTs offer a unique chance to revolutionize how different populations are included in investigations, and delegates are anxious to find the best way to proceed in this regard.

7 Precision Medicine

The rise of precision medicine, in oncology and other therapeutic indications, has tremendous consequences for how clinical studies are designed and conducted - particularly in light of novel technologies and DCTs. Peers are anxious to find ideas that translate to cost-effective investigation solutions, offering unique opportunities to deliver targeted therapies with life-saving potential.

8 Artificial Intelligence

Artificial Intelligence (AI) has touched upon every area of the pharmaceutical industry, and clinical development is no exception. From predicting patient responses, to providing artificial control arms, the potential is limitless - and peers hope to find solutions that are not only cost-effective, but can also accelerate their own timelines.

9 COVID-19

Alongside its other impacts, which are expected to be lasting, COVID-19 still directly impacts how we run clinical trials. Delegates are anxious to COVID-proof their own studies in the eventuality that novel variants emerge, while government stances towards the virus across the world still influence decisions - particularly policies such as China's willingness to re-enter lockdowns.

10 Real World Evidence

Real World Evidence (RWE) offers unique opportunities to gather data during clinical investigations, and many peers hope to leverage novel technologies to do so - while translating clinical insights gathered this way into useful information for future development efforts or into iterative optimization processes.

AI for Diversity in Clinical Trials - Insights from PharmaFEATURES

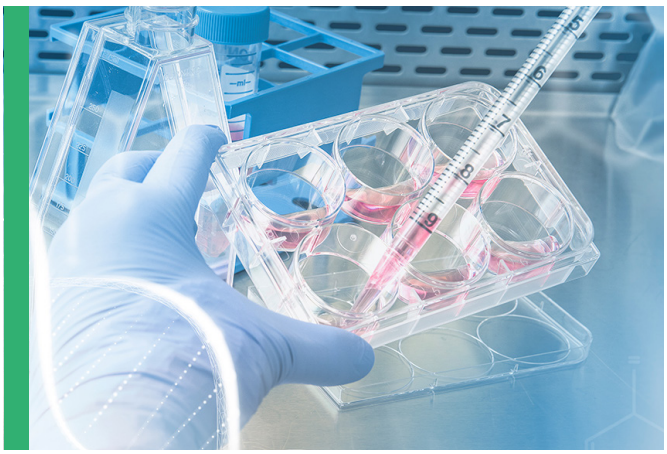
Clinical research continues to face calls to increase the diversity of patient pools. Regulators and patient advocacy groups all demand higher inclusivity in clinical development, but so does common sense: we should be developing drugs with the entire market, in its full diversity, in mind – not a restricted subset. However, reaching out to traditionally excluded and underserved groups is easier said than done. Artificial Intelligence (AI) has made significant forays into the life sciences in the last few years, and many are already examining how it can be employed to improve diversity in clinical investigations – as well as the conclusions that are drawn from them.

We examined the inherent need for diversity in an earlier article, highlighting obvious flaws in medical practice that were borne of a lack of inclusivity in research. These include the long-time association between UV exposure being a contributing factor for skin cancer incidence – something that later turned out to be untrue for many non-white populations. As we progress towards more personalized, precise medicine, it is more important than ever to be cognizant of how products will affect different populations.

Obstacles for Adoption

Traditionally, clinical trials have been heavily concentrated around large urban areas and hospitals that engage with cutting-edge science. Decentralized Clinical Trials already promise to expand the reach of clinical recruitment beyond this limited geography, while removing cost-related barriers such as having to travel to on-site facilities that are often remote for many populations – especially rural, older individuals. AI has a crucial role to play in expanding this reach. Integrated technologies can alert physicians, even those that are not habituated to keeping up-to-date with clinical trials, to the existence of suitable investigations for their patients.

IQVIA's Vice President for analytics, Lucas Glass, expounded on the subject of patient-matching in an interview with Medical Technology. The key takeaway is that algorithms are already well-suited to matching investigations with patients and ensuring they meet recruitment diversity goals. The problem remains finding a way to insert such matching to clinical workflows. Rolling out suitable technologies throughout the healthcare infrastructure and familiarizing healthcare practitioners with the clinical trial landscape that can offer real-term benefits to their patients will doubtlessly prove pivotal for success.



The Need for Ethical AI

One particularly crucial area of concern for AI in clinical diversity is how AI algorithms are built. While AI has shown potential in removing barriers to research and matching patients to trials that they otherwise would not have had access to, it can also perpetuate existing stereotypes. AI is non-moral, but it can inherit the prejudices of its creators, depending on how the model is constructed. For example, using nonrepresentative datasets to train machine learning algorithms can lead to skewed conclusions and a failure to account for factors such as sex, socioeconomic status, race, and others.

Use-cases of pulse oximeters serve as a good example for illuminating such biases. These are devices which measure blood oxygenation levels by shining light on skin; however, highly pigmented skin can scramble the light and lead to inaccurate readings in darker people. Unsurprisingly, a review of 130 medical AI device post-approval evaluations showed that less than 13% of these reported critical diversity markers such as sex, race or ethnicity. Considering that such medical devices form the backbone of AI model construction for clinical investigations – especially so when they are used at home in the context of a decentralized clinical trial, there is a clear need to do better.

Improving Outcomes for Underserved Populations

A study examined the benefit of training Natural Language Processing (NLP) models on gender-sensitive word embeddings to compensate for the overwhelming representation of men in existing clinical literature. The investigation concluded that NLP algorithms built this way demonstrated significantly improved performance – highlighting how AI can promote diversity as well as improve outcomes for less enfranchised demographics.

Other approaches have also included employing models to predict differences in adverse events across populations. These include AwareDX, a model employed to estimate adverse event variance between men and women. It has long been known that women take longer to metabolize most drugs – leading to higher bioactive pharmaceutical concentrations for a longer period of time. The investigators noted that sex could be replaced with other variables of interest to apply to different aspects of drug discovery – such as age, to differentiate adverse report analysis for pediatrics. Similar efforts will prove crucial in accommodating for increased diversity in clinical development, as well as successfully rolling out new products for diverse populations.

Addressing the AI – Diversity Interface

As the adoption of AI in clinical practice grows, and with good reason, we must strive to increase awareness of its vulnerability to bias. To do so, it is important that pressure is mounted on the part of regulators, funding agencies and publishers to meet diversity requirements. However, a broader educational approach is also needed – we must recognize the biases that we can engender in the models we construct, after all.

Artificial Intelligence presents the opportunity to improve patient recruitment through providing a greater geographical and social reach for clinical trial operators to recruit from – but this can only happen if the entire healthcare industry is engaged with the technology. The long-standing diversity gaps in clinical literature and datasets also present challenges for interpreting historical results and training AI models based on those. Models have already shown they are able to compensate for the biases present in such datasets, if their constructors are aware of them and program them accordingly. While AI offers unique potential in this area – it is not a panacea; as is often the case with diversity, change must first begin with us.

Read more on the latest trends in the life sciences industry on **PharmaFEATURES**

TOP Investment Areas 2022

Proventa asked delegates at its events to speak about their investments for the coming year. Patient recruitment and the challenge of coping with novel technologies, complex trial designs and decentralized clinical trials featured high on the list as the industry comes to terms with the lasting impact of the pandemic.

Patient Recruitment

Recruitment overall is of prime concern to delegates in a post-pandemic world. More specifically, delegates are pouring resources into recruiting the right patients, particularly with the rise of precision medicine where treatment response is becoming a more crucial aspect of investigation.

Site Selection

As decentralization rises in prominence, many peers are rethinking the location of their traditional physical sites to provide for the maximum, most diverse recruitment and retention efforts as well as save on costs and time.

Clinical Trial Logistics

Providing increased resilience to supply chains is of paramount importance, in a world which has shown us just how fragile these can be in times of need. Many delegates are investing in the area, while excitement for improved tracking and accountability systems also abounds. Novel technologies such as blockchains in supply chain management are also expected to make an impact in the near future.

EDC / CTMS

Electronic Data Capture and Clinical Trial Management Systems (EDC, CTMS) are rising in prominence, particularly as sponsors encounter more complex design protocols and the need to comply with higher standards, new regulatory requirements, data storage and privacy concerns. Investments in the area are expected to continue as DCTs grow further in importance.

Consulting

Given the uncertainties faced by the industry over the last two years, it should be unsurprising that many peers are investing heavily in consulting services to assist them in navigating the new reality in the clinical operations space after the pandemic. With many new developments to tackle, such as DCTs, Patient Centricity, Diversity and Inclusion and improved good practice expectations, this is expected to continue.

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eTMF

Electronic Trial Master Files (eTMF) are not yet essential, but are mandatory for Good Clinical Practice (GCP). eTMFs simplify compliance and improve the ease of collaboration regardless of location, as well as providing added security and accountability throughout the clinical trial life cycle. Investment and adoption in this area is likely to continue as peers seek to simplify their own working environments.

Real World Evidence

Gone are the days when Real World Evidence (RWE) was thought of as a "ruby in the rubbish" approach that rarely yielded meaningful results rather than garbage. The potential to harness smart technology and wearables for legitimate and valid clinical insights is now widely recognized, and peers are investing appropriately in the technology.

Patient Engagement

Maintaining patient engagement can often mean the difference between success and failures, and delegates are investing resources in ensuring constructive, trust-building relationships with their patients. Digital support platforms provide a unique way to achieve this, and remote technology is thought to be of foundational importance in the future of patient engagement.

Risk Based Monitoring

Delegates cited a need to invest in improved Risk Based Monitoring (RBM), the overall umbrella term under which Risk Based Quality Monitoring (RBQM) falls under. The data-driven approach to minimize risks and prevent liability frees up time to focus on higher-value tasks, avoiding the need for 100% source data verification. Peers see the potential for cost-efficiency.

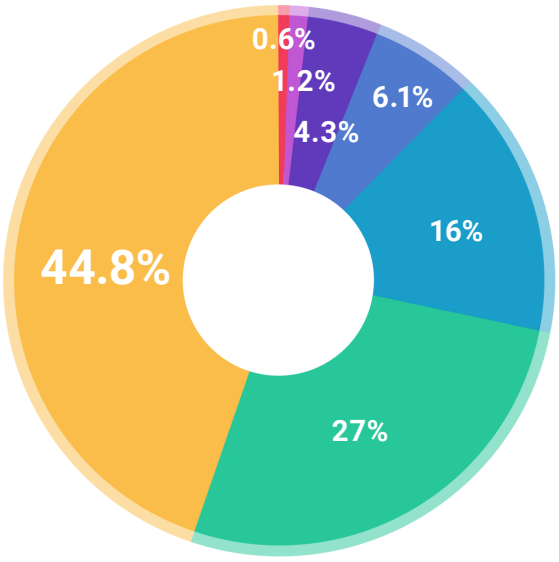
Virtual Trials

Investments in virtual trial technology are naturally on the rise, as peers seek to add DCT elements to investigations - whether that be full or partial decentralization. Smart technologies improve recruitment, engagement and increase safety, all the while minimizing long-term costs if implemented appropriately.

Delegate Breakdown:

Attendees at Proventa's 2022 Strategy Meetings

2022 Atendee Breakdown



44.8% Director level

27% Team Lead

16% Vice President

6.1% C-level

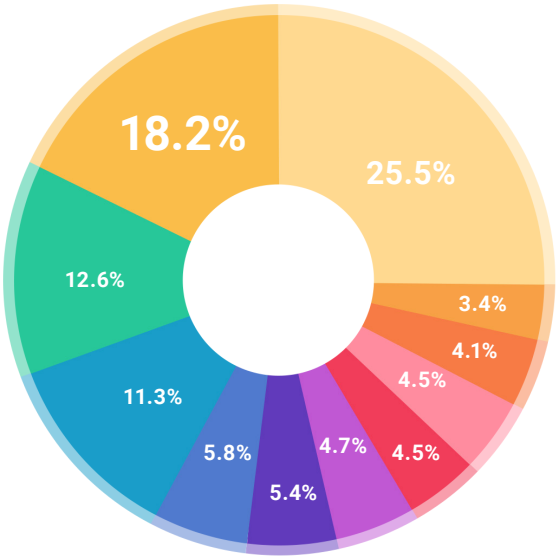
4.3% Scientist

1.2% Other

0.6% Academia

Drug Development Stages

Therapeutic Areas



- Oncology
- Rare Diseases
- Immunology
- Infectious diseases
- CNS
- Haematology
- Neurology
- Inflammation
- Cardiovascular
- Metabolic diseases
- Other

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