

# Clinical Researcher

**The Authority in Ethical, Responsible Clinical Research**

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**Not Just Numbers: Big Data, Artificial Intelligence, Real People**

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## Clinical Researcher

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CHAIR'S MESSAGE

**Flying High, and Touching Down Again with a Mission in Mind**

Christine Senn, PhD, CCRC, CPI, FACRP, 2023 Chair of the Association Board of Trustees



The ACRP 2023 conference did not disappoint! Nearly 1,400 attendees were flying high after our frankly joyous and inspirational time together in Dallas in late April and early May. As I first walked into the main level of the convention center, an overhead banner proclaiming it was “The Place to Be for Clinical Research Professionals” set the stage for what proved to be absolutely true.

Many wonderful conferences happen throughout the year in our industry, and I am a fan of countless of them. It is ACRP, though, that lives a mission that I hold dear: “representing, supporting, and advocating for clinical research professionals.” Frankly, the clinical research enterprise needs advocates and, more pointedly, it needs us to advocate for why ours is a true profession.

**For Learning**

We range from trainees to seasoned professionals with varied specialties of knowledge. I am a diehard advocate of ACRP certification because it showcases a person as a clinical research professional. A wonderful moment for me was when ACRP expanded its certifications beyond clinical research coordinators, associates, and principal investigators to include the tens of thousands of people who do this work alongside those heroes from their places in the lab, pharmacy, administration, regulatory bodies, contracts and budget departments, along with protocol design, statistics, and so much more. That’s precisely what it means to be “the place” for clinical research professionals! All of us, in every domain, are represented and have the opportunity to earn trust-engendering certifications once a solid level of understanding is achieved.

ACRP also supports our industry's important endeavors—such as striving for greater diversity in both our workforce and in patient recruitment. Last month, in the days leading up to the May 20 celebration of [Clinical Trials Day](#), former Association Board of Trustees Chair Dr. Dave Morin, former Association Board of Trustees Treasurer Sergio Armani, and Scott Chatterton donned snazzy cycling gear and flexed their calves across nearly 355 miles of trails in Pennsylvania, Maryland, and the D.C. area to raise \$79,375 from more than 120 corporate sponsors and individual donors for ACRP diversity initiatives through the third annual [Ride4DEI](#). Joining in the effort on the West Coast was Justin Chia, who essentially mirrored the trio's journey on a variety of California trails.

Donations to Ride4DEI supported 20 event scholarships for ACRP 2023 attendees from underrepresented groups selected by the ACRP [Diversity Advisory Council](#), and such backing is expected to make scholarships available again next year! I was also delighted to see a great number of friends from the Latinos in Clinical Research and Black Women in Clinical Research organizations show up in Dallas this year. The energy was electric!

### **For Listening**

Another critical endeavor concerns our workforce in general. The number of clinical trials, as well as their complexity, increases year after year, and there simply are not enough people to fill all the jobs available. Every conference in our industry fosters learning and offers forums to share best practices, and I certainly heard exclamations about how great the ACRP 2023 sessions and networking opportunities were as I walked by other inspired attendees. What I also had the privilege of experiencing, though, was an [all-day workshop of leaders in the field](#) coming together to share and brainstorm ideas about how to develop career paths into clinical research at the high school, college, and university levels, as well as how to train newcomers most effectively so we develop our workforce to meet the needs of our industry. There is truly wonderful work being done in [workforce development](#) at ACRP.

I started this note saying the time at the conference was joyous and inspirational. Happy, excited faces brimmed both in person and on social media, with an infectious buzz! I witnessed so many people say how energized they were, saw them make plans to join Chapters and attend more events,

and heard them express great interest in keeping conversations going beyond the conference. In that way, I felt surrounded by the inspired energy of others.

My own inspiration came from the number of attendees during and after the conference who asked me how they could [get involved as an ACRP volunteer](#). It takes hundreds of volunteers each year to decide the conference's content (Content Committee), handle ethical issues (Ethics Committee), find and interview candidates to serve on our boards (Nominations Committee), actually serve as trustees (both on the Association Board of Trustees and on the Academy Board of Trustees), and write questions for the various certification exams. Opportunities abound to both increase your knowledge and promote the knowledge of others, and [the nominations period for service in 2024 is now open](#) through the end of June for the boards and until September 15 for committees!

### **For Life**

Together, there is much we can accomplish for all the stakeholders in our clinical research enterprise in the second half of 2023 and in the already-bubbling buildup to our ACRP 2024 conference in Anaheim, Calif. I hope to see many of you again, or for the first time, as more ACRP events come along this year, or next spring as I get to see what attending the conference is like as an immediate-past Chair of the Association Board of Trustees. In the meantime, you have my thanks and encouragement for your dedication to helping others in our industry fly high and to fulfilling the mission set before us.



PEER REVIEWED

## **Forward Thinking for the Integration of AI into Clinical Trials**

Brian Mai; Andrea Roman, MS; Alondra Suarez, MS



Streamlining pain points of the clinical trial process to reduce costs and improve patient results can be accomplished with artificial intelligence (AI). For example, AI can support patient recruitment and retention by seeking potential participants and foreseeing the probability of subject withdrawal. Patient monitoring can be improved by collecting real-time data using wearable devices and sensors on the patient's physiological parameters. These data can be analyzed using AI to identify patterns indicating the start of potential adverse events or complications. Furthermore, AI can help data quality by lessening the effects of confounders and expanding the scope of use for AI wearable technology.

Further, deep learning models can be trained to continuously analyze and interpret patient data for individual patients and across cohorts. This allows researchers to uncover patterns that may otherwise have been unrecognizable.

In this paper, we examine how, although there are challenges and drawbacks to implementing AI in clinical trials, it has potential benefits that make it a viable tool for the pharmaceutical industry.

### **Background**

AI has become increasingly prevalent in the healthcare industry, with one area of application being in clinical trials for pharmaceutical products, which are time consuming, expensive, and labor intensive. Indeed, clinical trials require a large investment of resources, and it takes years to bring a drug to market.

Part of the issue is due to the frequent failure of clinical trials, which, when they occur, come extremely late in the overall development cycle for a drug. Only around 10% of drugs entering the clinical trial stage eventually receive U.S. Food and Drug Administration (FDA) approval. The failures of the other 90% are often ascribed to poor patient cohort selection, recruiting tactics, and insufficient infrastructure to support complex clinical trials. { 1 }

In such a challenging environment, AI can be leveraged to streamline various aspects of the clinical trial process, such as patient recruitment, data analysis, pattern recognition, and identification of potential adverse events. Researchers could expedite the drug development process, potentially reducing costs and improving patient outcomes. However, as with any new technology, there are hurdles to overcome and drawbacks to be faced when implementing AI in clinical trials.

## **An Overview of AI**

AI is a branch of computer science that aims to create intelligent machines that can perform tasks that typically require human intelligence, such as visual perception, speech recognition, and decision making. One of the critical components of AI is machine learning, a subset of AI that involves algorithms and statistical models to enable machines to learn from data and improve their performance over time.

Deep learning is a subfield of machine learning that uses artificial neural networks with multiple layers to learn complex patterns in data. Neural networks are a set of algorithms that are modeled after the structure and function of the human brain. They consist of layers of interconnected nodes or neurons that process information and make predictions based on input data. Neural networks are commonly used in deep learning applications, and can be trained to perform various tasks, including image and speech recognition, natural language processing, and decision making. { 1 }

## **Current Uses of AI in Clinical Trials**

AI can improve patient recruitment by *identifying and screening potential participants* based on inclusion and exclusion criteria. This can help reduce the time and cost associated with patient recruitment, which is a common clinical research issue.



Once the trial is under way, *patient monitoring* can be improved by incorporating the use of AI, which in turn can help improve patient safety and reduce the risk of adverse events. For example, AI algorithms can detect and predict adverse events by analyzing various data types, such as vital signs and patient-reported outcomes. This can help researchers identify potential safety concerns more quickly and take appropriate action, such as modifying the study protocol or adjusting the dosage of the drug being tested.

Additionally, wearable devices and other sensors can collect real-time data on patients' physiological parameters, which can be analyzed using AI to identify patterns indicating the onset of a potential adverse event or complication. In short, AI can help improve patient monitoring during clinical trials, leading to better patient safety and more efficient drug development.

Meanwhile, the majority of clinical trials experience some level of subject dropout. There are various ways that AI could improve *subject retention*. This could involve using AI to identify factors associated with a high risk of patient dropout. AI models could be used to predict the probability of subject dropout, which would allow researchers to be proactive in subject outreach. This could significantly decrease the resources and time restraints associated with clinical trials. Furthermore, wearable technologies, such as an Apple Watch or Fitbit, combined with AI, could improve both subject retention and monitoring.

It is important to note that clinical trial participants are not in a completely controlled environment. Studies must be planned with factors such as loss to follow-up and variability of self-reported patient data in mind. AI allows researchers to minimize the effects of such confounders and improve data quality.

Researchers could combine AI with wearable technologies to simplify self-reporting data collection, as patients would only have to wear the technology that gathers the appropriate biological data rather than manually collecting the data. This could expand the scope of use for wearable technologies in clinical trials as AI could be trained to analyze this data in real-time and improve adherence to the study protocol. Offering another way to mitigate issues related to data reliability will help ensure the collection of complete datasets. Of the various AI methods, deep learning can be used to analyze data collected by wearable technologies and diagnostic devices.

## AI Software and Tools

*Deep learning* is a class of machine learning methods based on artificial neural networks that mimic information processing and distributed communicated nodes in humans. The neural networks use multiple layers to extract higher level features from input progressively. {2} Deep learning models can be trained to continuously analyze and interpret patient data for an individual patient and across cohorts, while automatically adjusting to disease expression and treatment response changes. This tool will allow researchers to learn from complex datasets and uncover patterns that may otherwise have been unrecognizable.

In a 2015 study, Shah, et al. evaluated the efficacy of clinical outcomes generated from technology-enabled non-invasive diagnostic screening (TES) using smartphones and other point-of-care medical sensors versus conventional vital signs examination. TES synergistically identified clinically significant abnormalities in subjects who presented as usual in routine health screenings. Physicians verified TES findings and used routine health screening data and medical history responses for comprehensive diagnoses for at-risk patients. The researchers concluded that, while routine health screening continues to be necessary, the emerging techniques of TES can play an essential supporting role in the early detection of disease, continuous monitoring throughout clinical trials for adverse events, and providing personalized screening and care to support clinical trials. {3}

A second study evaluated an AI system that continuously analyzes arterial pressure waveform during surgery and warns if hypotensive events are expected within the next 15 minutes. The researchers concluded that this study demonstrated that using AI compared to standard care resulted in less intraoperative hypotension. {4}

These two studies demonstrate the applicability of AI methods for real-time analysis of clinical data and for early detection of adverse events in clinical trials. While physicians must still provide standard patient care, AI can help physicians and researchers detect the onset of abnormalities and adverse events much sooner. Thus, AI methods offer a cost-effective and rapid solution to improve patient outcomes in clinical trials.

AI's language compatibility is an additional tool for scouring data across the web quickly thanks to *natural language processing* (NLP). Like human comprehension, a device can be programmed to

understand written or spoken words. Within the medical practice, this can be used to read through physicians' comments and pathology reports to determine if the patient meets the eligibility requirements to enter a specific clinical trial.

With the help of NLP, researchers devised an AI tool called Criteria2Query, which standardizes inclusion and exclusion criteria within databases and allows professionals to gather information simplistically without needing extensive context. Another AI creation, made by the same researchers, involves searching from the patient's perspective.<sup>{5}</sup> ClinicalTrials.gov can be a daunting database for those unfamiliar with what to look for in a trial. Hence, DQuest, another AI NLP tool, generates a series of dynamic questions for patients to answer and then filters their options based on the responses. While the accuracy could improve, an initial study showed that it could exclude 60% to 80% of trials for which the patient was not eligible. Allowing patients to select their trials could increase satisfaction and retention rates.

### **HIPAA, Patient Privacy, and Patient Rights**

With the Health Insurance Portability and Accountability Act (HIPAA), patients have the right to privacy and control over their personal health information (PHI), including the right to access their personal health files, petition for corrections, and be informed about how their PHI is disclosed and used.<sup>{6}</sup> Researchers and healthcare organizations must comply with HIPAA regulations and as well as other privacy laws to ensure patients' PHI is protected.

Utilizing AI technology in patient recruitment can lead to more challenges in ensuring compliance with these regulations. For example, AI algorithms may need to access a large amount of patient data to identify appropriate clinical trials. However, these data must be de-identified and protected to ensure patient privacy and prevent unauthorized access to PHI. Additionally, third-party organizations in AI-driven patient recruitment have the potential to create other risks to patient privacy and compliance with privacy regulations.

Healthcare professionals and researchers must prioritize compliance with HIPAA and other privacy regulations to ensure that patient data are de-identified and protected, as well as put appropriate safeguards in place to prevent unwanted access to PHI. Lastly, they must ensure that third-party

organizations involved in AI-driven patient recruitment are in compliance with HIPAA and other privacy regulations.{7}

To address these concerns, patients and subjects should be provided with clear and concise information about how AI technology is used in patient recruitment. This includes how their PHI will be used and protected. Researchers must work to build trust with patients and subjects by highlighting the potential benefits of using AI technology in clinical trials while also being transparent about potential concerns and risks.

By prioritizing compliance with privacy regulations and patient and subject education, researchers and organizations can maximize the potential benefits of AI technology while ensuring that patients and subjects have confidence and are informed about participating in clinical trials.

### **FDA Regulations and Revisions**

The FDA has been following an action plan for AI use in medical devices. It involves a series of proposed measures the agency would take in response to stakeholder feedback from an initial outline of regulatory modifications.{8} Most recently, the FDA has issued an updated revision of its guidance document for the “Predetermined Change Control Plan for AI/[Machine Learning]-Enabled Devices,” which highlights and defines for device manufacturers “what” changes are being made to the device using machine learning and “how” the changes in algorithms will be redeveloped to still maintain safety and efficacy.{9}

In addition, the FDA is taking action to ensure the harmonization of Good Machine Learning Practices (GMLP), which will focus on removing bias from AI algorithms and enforce a standardized system for scouring patient health records. To maintain transparency with patients, the FDA hosts public workshops with the Patient Engagement Advisory Committee on how device labeling can foster transparency between manufacturers and users while also building trust in AI medical devices. Stakeholders were concerned about bias within AI algorithms and suggested better methods to ensure validity.

The FDA will back regulatory scientists in their methodology and research on exploring, identifying, and eliminating bias within AI. The FDA was also asked to clarify what “real-world performance”

would look like for AI devices. In response to that, they will be working together with stakeholders that are piloting this application.

## Conclusion

The future of the use of AI in clinical trials is promising. While personal AI hardware could cost upwards of \$10,000 to \$4 million for building complex language processing systems, there is still zero cost to use open-source options that can give worthwhile results. There are still safety and efficacy concerns over AI, but the new hope is that clinical trial data interpretation will become a faster, more efficient, and reliable system with the help of technological advancements. The progress of patient care will open new doors for personalized medicine and allow inclusivity and transparency for patients of all backgrounds and medical needs to be involved in clinical trials. AI is not meant to replace clinical trial professionals, but rather to supplement the work that is being done to support the development of groundbreaking medical products, which will positively impact countless lives.

## References

1. Harrer S, Shah P, Antony B, Hu J. 2019. Artificial Intelligence for Clinical Trial Design. *Trends in Pharmacological Sciences*. <https://pubmed.ncbi.nlm.nih.gov/31326235/>
2. Zhou Q, Chen Z, Cao Y, Peng S. 2021. Clinical Impact and Quality of Randomized Controlled Trials Involving Interventions Evaluating Artificial Intelligence Prediction Tools: A Systematic Review. *NPJ Digital Medicine*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8553754/>
3. Shah P, Yauney G, Gupta O, Patalano II V, Mohit M, Merchant R, Subramanian SV. 2018. Technology-Enabled Examinations of Cardiac Rhythm, Optic Nerve, Oral Health, Tympanic Membrane, Gait and Coordination Evaluated Jointly with Routine Health Screenings: An Observational Study at the 2015 Kumbh Mela in India. *BMJ Open*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5914894/>
4. Wijnberge M, Geerts BF, Hol L, Lemmers N, Mulder MP, Berge P, Schenk J, et al. 2020. Effect of a Machine Learning-Derived Early Warning System for Intraoperative Hypotension vs Standard Care on Depth and Duration of Intraoperative Hypotension during Elective Noncardiac Surgery: The Hype Randomized Clinical Trial. *JAMA*. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7078808/>
5. Woo M. 2017. An AI boost for clinical trials. *Nature*. <https://pubmed.ncbi.nlm.nih.gov/31554996/>
6. Health Insurance Portability and Accountability Act of 1996. Centers for Disease Control and Prevention. <https://www.cdc.gov/phlp/publications/topic/hipaa.html>

7. Sharing and Utilizing Health Data for AI Applications (Roundtable Report). Center for Open Data Enterprise. 2019. <https://www.hhs.gov/sites/default/files/sharing-and-utilizing-health-data-for-ai-applications.pdf>
8. Artificial Intelligence/Machine Learning (AI/ML)–Based Software as a Medical Device (SaMD) Action Plan. 2021. FDA Center for Devices and Radiological Health. <https://www.fda.gov/media/145022/download>
9. Predetermined Change Control Plans for AI/ML–Enabled Devices. 2023. FDA Center for Devices and Radiological Health. <https://www.fda.gov/medical-devices/medical-devices-news-and-events/cdrh-issues-draft-guidance-predetermined-change-control-plans-artificial-intelligencemachine>



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CULTIVATING QUALITY

## Putting the Patient First is Integral to Building a Strong Quality Culture

Londa Ritchey, MS, MBA



Understanding the needs of your customers and getting them right the first time builds customer satisfaction and a sustainable business strategy. That seemingly simple objective is at the heart of a strong quality culture.

For the pharmaceutical industry, this means ensuring medicinal therapies reach patients in accordance with the elements of safety, efficacy, and timing that are expected. To achieve that and build a strong quality culture, organizations must align all business objectives, decisions, and actions around this overarching focus.

A strong quality culture focuses on assessing patient safety in all aspects and decisions of the company, not just within the quality department. Patient safety should be paramount in all decisions, big and small. For example, a seemingly simple change of secondary packaging components can result in vial breakage or cracks and could result in a product recall. GxP changes such as these require all functions within the organization to consider the potential patient safety impact from their daily processes and decisions.

### Why Management Matters

A strong quality culture is influenced by its leaders. As such, management should “walk the talk,” setting goals and objectives aligned with building and sustaining that culture.

Quality culture is defined by the behavior and decision-making hierarchy outlined by the company leadership. This includes setting the goals, strategic objectives, and metrics on which the performance of the organization is assessed. Rewards for accomplishment are key to assuring the proper processes that force risk-based and cross-functional decision-making. As an example,

rewards should be based on identifying and communicating issues early or completing activities correctly the first time, with all proper controls and checks executed as expected.

Quality culture puts processes in place to allow decision-making when senior management is not available. Will the tactical operators be able to actively identify issues as they occur, or will they become passive if accountability is with the management team only?

Team members across all levels of the organization should be capable of making decisions on patient safety or raising concerns about it.

Complex operations within biopharma and cell and gene therapy mean missteps will occur. To mitigate the impact of this, personnel should be empowered to speak up if they identify any issues that could impact patient safety. Empowering and rewarding team members for diligent identification and reporting of mistakes, and for offering potential solutions, helps to mitigate risks to patient safety. This empowerment requires management to support continuous education about patient safety risks within the operation.

### **Recruiting the Right People**

A cross-company quality focus depends on having people with the right skills. That begins with hiring by defining the skills needed and ensuring candidates' skills match the organization's quality culture objectives. Job descriptions should include core critical skills the organization requires. These include skills related to a strong quality culture, such as critical thinking skills, continuous improvement mindset, and cross-functional thinking.

Once hired, employees should receive continuous GxP training related to their specific function. Patient safety risks associated with the function must be at front and center of that training. To ensure the quality culture shapes the business at every level, employees must also be trained to identify potential patient safety risks within their functions and know how to escalate these for visibility and remediation.

Potential team members should be made aware of the organization's emphasis on building a solid foundation of quality culture competency.



Build an assessment tool to better understand the potential candidate’s skill level, including their quality culture acumen. Quality culture–related discussion points during candidate interviews, for example, could include “describe your understanding of quality culture”; “provide an example of when you have made a patient safety decision”; and “explain the patient safety impact of your previous role.”

## **A Quality Education**

Focus on quality culture should continue through onboarding and continuous training initiatives, including the sharing of patient stories and dealing with unplanned outcomes.

Teach new team members to look for error traps and patient safety concerns and to feel safe sharing these discoveries. Expect them to assist in error-proofing the processes and reward such contributions.

As part of continuous training, share lessons learned when things do not go according to plan. Focus on the patient safety concern associated with any issues and the risk-based thinking that should be applied in any similar future situations. Use examples of noncompliance concerns other companies are experiencing within industry by utilizing shared internet resources. Share these as lessons learned to proactively avoid the same issue.

Personnel must believe management expects and rewards learning and sharing ideas to strengthen quality culture. This requires building training time into the daily schedule. Additionally, performance metrics should link to on-time training completion for core-function training requirements.

## **Conclusion**

Patient safety must be integrated into everything a pharmaceutical company does. Having a strong, enduring quality culture will help to achieve that objective while also building a resilient business and workforce.



**Londa Ritchey, MS, MBA**, is Quality Director with the Quality Management and Compliance group at [PharmaLex](#).

DEI BY DESIGN

## Designing High-Impact Clinical Trials That Serve Patients, Clinical Centers, and Industry Sponsors

Erin Leckrone, MFA, MBA



Clinical trials are critical in developing effective and safe new treatments and improving patient outcomes. When well-designed and managed, they benefit participants, investigators, trial sponsors, and the entire medical community. They are vital to the advancement of the science of cellular therapy, including hematopoietic cell transplantation (HCT). Approximately 25,000 treatments and outcomes involving HCT or cellular therapy for cancer and other life-threatening disorders are reported to the CIBMTR<sup>®</sup> (Center for International

Blood and Marrow Transplant Research<sup>®</sup>) annually, a number that increases by about 5% per year.<sup>{1}</sup> However, trials in the HCT space have complex challenges that impact the clinical trial sponsors, investigators, clinical trial sites, physicians, patients, and their caregivers, ranging from trial design to patient or donor selection to long-term follow up.

### Expanding Access

When patients understand all their treatment options—including clinical trials—they can make informed decisions. However, it can be difficult for patients to find and join clinical trials and, all too often, ethnically diverse populations are underrepresented. Widespread participation in clinical trials across populations is essential to ensure scientific innovations are safe and effective for all patients who may need therapy.

A recent analysis by the Blood and Marrow Transplant Clinical Trials Network, which focuses on clinical trials for HCT and cellular therapy, demonstrates the widespread challenge of ensuring ethnically diverse patient enrollment in clinical trials. The organization analyzed and compared the race and ethnicity of the patients enrolled in nine clinical trials spanning 2014 to 2021 to the race and ethnicity of the total United States population using 2020 census data, all potentially eligible HCT recipients at participating trial centers at the time of trial enrollment, and all potentially eligible HCT recipients at all transplant centers in the United States at the time of trial enrollment.

In all but one trial, the proportion of underrepresented racial and ethnic group participants was lower than the general population. In six of the nine trials, the proportion of participants from such groups was lower than those potentially eligible at the participating centers.<sup>{2}</sup> This analysis contained valuable lessons on improving clinical trial participation.<sup>{3}</sup>

There are a number of organizations that provide resources for patients, clinical sites, and industry sponsors. The National Marrow Donor Program/Be The Match's Clinical Trials Search and Support Program includes a searchable clinical trial database, one-on-one support, financial grants, and patient resources in plain language.

In addition, clinical research organizations (CROs) can take steps to broaden access to trials, including:

1. Prioritizing and routinely monitoring diversity in the clinical trial accrual plan.
2. Broadening eligibility criteria even further.
3. Collaborating with advocacy organizations and community groups.
4. Helping patients understand clinical trials.
5. Making it easy for patients to comply with follow-up assessments.
6. Using diversity resources to identify opportunities for improvement.

Finally, ongoing research can help address this gap, specifically when it comes to eligibility. For example, many allogeneic HCT clinical trials require a patient to have a fully matched (8/8) donor to enroll. The chance of having a matched, available unrelated donor on the Be The Match Registry<sup>®</sup> varies significantly depending on a patient's ancestral background, and currently ranges from 29% for Black and African American patients to 79% for non-Hispanic white patients.{4}

A recent clinical trial demonstrates what can happen when eligibility criteria expand beyond fully matched donors. Known as the 15-mismatched unrelated donor (15-MMUD) trial (NCT02793544), it assessed the safety and efficacy of using bone marrow from MMUDs in combination with PTCy graft-versus-host disease (GVHD) prophylaxis. The researchers concluded this approach was safe and effective and could significantly expand HCT access, especially for those who are ethnically diverse. In addition, the researchers noted 48% of patients enrolled in 15-MMUD were ethnically diverse, which is almost double the typical enrollment in HCT clinical trials.{5}

CROs and sites must work together to improve diversity in clinical trial enrollment in all areas of medicine to advance health equity for racially and ethnically diverse patients.

### **Collaborative Expertise**

A collaborative approach to cell therapy clinical trial challenges pushes the boundaries of discovery and speeds life-saving treatments to patients. When organizations collaborate, sponsors can leverage unique expertise, unparalleled resources, and an established, stable infrastructure, including research, sites, donors, partnerships, and scientific and operational expertise. As a result, the time required to design, launch, and execute high-impact clinical trials is significantly reduced.

This collaboration can span the clinical trials continuum that starts with clinical trial design and management focused on the patient experience and ends with outcomes collection, research, and long-term follow-up. It also includes search and support services that help patients understand, find, and enroll in clinical trials. This type of collaborative nature helps ensure the successful execution of internally sponsored, industry, and academic studies and gives many patients access

to life-saving treatments. One example of this type of collaboration among industry, academia, and CROs relates to the approval process for abatacept.

In December 2021, the U.S. Food and Drug Administration (FDA) approved abatacept for the prevention of acute graft-versus-host disease (aGVHD) for patients aged 2 and older who received a matched or mismatched unrelated donor (MMUD) transplant. It is the first FDA-approved drug for the prevention of aGVHD and will increase access to HCT for more patients with hematologic malignancies and disorders.

The FDA based its approval on the safety and efficacy data from two separate studies: the Phase II clinical trial GVHD-1 (also known as ABA2){6} and a confirmatory observational study, GVHD-2.{7} Our CIBMTR CRO Services prospectively supported the GVHD-multicenter ABA2 study that included a double-blind, placebo-controlled cohort and an open-label, single-arm cohort. The GVHD-2 study used real-world data provided by CIBMTR to further evaluate the impact of abatacept on the survival of HCT recipients with a 7/8 MMUD.

The CIBMTR CRO Services is supporting the currently enrolling ABA-3 trial (NCT04380740). This multicenter, randomized, double-blind, Phase II trial is investigating extended dosing of abatacept in MMUD recipients with a goal to reduce the risk of chronic GVHD.

### **Challenges and Complexities on the Road to Innovation**

Clinical trials are critical to improve outcomes for patients and advance the science of life-saving cell therapies. With the unique challenges and complexities of these innovative treatments, academic and industry sponsors can benefit from the synergies offered by industry organizations and nonprofits that include:

- End-to-end clinical trial design, operations, and logistics support.
- Built-out clinical infrastructure with a single institutional review board, dedicated data and safety monitoring board, master contracts, and technology that is compliant with the expectations of 21 CFR Part 11 in the *Code of Federal Regulations*.
- Access to patients and allogeneic donors for research.

- Models, analyses, and interpretations to help sponsors define their targets.
- Direct link to the CIBMTR Research Database with information on more than 630,000 patients.
- Industry-leading infrastructure to collect and analyze patient outcomes data.

## Conclusion

With careful planning, execution, and patient support, cell therapy clinical trials will pave the way for new treatments for all patients and may serve as a model for best practices in other areas of medicine.

## References

1. [Blood and Marrow Transplant Clinical Trials Network \(BMT CTN\) Annual Report](#), May 2021 - April 2022.
2. Horowitz MM, Kaur M, Mendizabal A, et al. 2022, [Racial and ethnic diversity on Blood and Marrow Transplant Clinical Trials Network \(BMT CTN\) trials — We can do better](#). *Transplant Cell Therapy* 28(3):S71. doi:10.1016/s2666-6367(22)00244-5
3. DeSalvo A, Horowitz MM, Lee C. Diversifying Enrollment in Clinical Trials: Where We Are, Where We Need to Be and How to Get There. *The ONE Forum* 2022.
4. Auletta J. 2022. Mismatched Unrelated Donors Expand Transplant Access to Diverse Populations. *Hematology Advisor*.
5. Shaw BE, Jimenez-Jimenez AM, Burns LJ, et al. 2021. National Marrow Donor Program–Sponsored Multicenter, Phase II Trial of HLA-Mismatched Unrelated Donor Bone Marrow Transplantation Using Post-Transplant Cyclophosphamide. *Journal of Clinical Oncology* 39(18):1971–82. doi:10.1200/JCO.20.03502
6. Bristol Myer Squibb. 2021. U.S. Food and Drug Administration Approves Orenicia® (abatacept) in Combination with a Calcineurin Inhibitor and Methotrexate for the Prevention of Acute Graft Versus Host Disease (aGvHD). <https://news.bms.com/news/details/2021/U.S.-Food-and-Drug-Administration-Approves-Orenicia-abatacept-in-Combination-with-a-Calcineurin-Inhibitor-and-Methotrexate-for-the-Prevention-of-Acute-Graft-Versus-Host-Disease-aGvHD/default.aspx>



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## Improving Access and Participation in Clinical Trials Using a Patient-Centered Digital Health Platform

Prof. Frank Sullivan, MB, MRCPI, FFRRSCI, MSc



Across Europe, we continue to see a declining trend in the number of clinical trials taking place, most notably since the European Union Clinical Trials Directive (CTD) was established in 2004. Among other countries, the decline in clinical trials in Ireland is a major concern, as it means that fewer people are given access to potentially life-saving treatments. This can have long-term effects on the quality of care being provided, as well as making it harder for new treatments to be developed and tested.

The CTD has had long-felt ramifications for all European patients and clinical researchers, with regulatory burdens and insurance requirements growing even more burdensome as time passed. At the same time, the global COVID-19 pandemic also affected the number of clinical trials, which [decreased by 19.6% in Europe](#) between August and October of 2020 compared to 2019. However, the effects of this decrease in access to clinical trials are being felt more severely in countries like Ireland, which have far fewer trials than their peers.

In this article, we explore the causes of decreased access to ground-breaking trials in Ireland and how to improve the quality of healthcare to create a healthier, more efficient system that better serves the Irish population.



## **The Current Landscape of Research in Europe and at Home in Ireland**

Despite Ireland's significant spend in its healthcare system, diverse population, and [heavy inbound investment from the pharma and med-tech sectors](#), the country is not able to keep up with its European counterparts in terms of clinical trial participation. According to the Central Statistics Office of Ireland, foreign direct investment in Ireland increased by €109 billion to €1,208 billion in 2021, a large proportion of that coming from the pharmaceutical and med-tech sectors. Compared to Finland and Denmark, which both have similar populations and economic wealth, [Ireland has only seen 18% of the 2,290 clinical trials](#) conducted between 2013 to 2021 in the three countries. In contrast, Finland and Denmark have respectively seen 29% and 53% of these clinical trials.

Ireland is not alone; the number of clinical trials in the United Kingdom (UK) has also declined significantly in recent times, with the Association of British Pharmaceutical Industry reporting that the number of industry-backed clinical trials started in the [UK each year fell by 41% between](#) 2017 and 2021. This steep drop is due largely to a combination of factors, including slow set-up times, increased staff fatigue and turnover, and a reduction in research capacity in the UK National Health Service. Unfortunately, this means that the UK and Ireland are lagging behind many of their European counterparts in attracting clinical trials.

The main barrier for Ireland when it comes to clinical trials is the need for more resources, both in terms of funds and personnel. Clinical trials require a significant amount of time from both researchers and practitioners to be successful. However, due to budgetary constraints, they are often forced to make do with limited personnel or wait for additional funding. Further, the infrastructure needed to support clinical trials is often expensive and difficult to obtain.

### **Addressing Barriers in the Current Clinical Trial System**

#### *Bureaucratic Impediments*

To reverse the trend of declining clinical trials in Ireland, the government has taken steps to address the administrative barriers to clinical trial participation in the country. One significant improvement is the centralization of ethics and standardizing the clinical trial process. The

National Clinical Trials Office (NCTO) was established to facilitate clinical trial research in Ireland. The NCTO provides a centralized infrastructure to support the set-up and management of clinical trials, including a clinical trial management system (CTMS), which allows researchers to track patient recruitment, trial progress, and data management.

### *Private-Public Expansion*

Through the Health Research Board infrastructure, Ireland has invested heavily in clinical research facilities, generally based in and around the public hospital university system, but penetration in the private healthcare delivery system is patchy at best. Up to one half of the Irish population carries healthcare insurance and receives some or all of its healthcare in the private system. There is clear scope to expand the pool of patients accessing trials, through measures designed to include all eligible patients, treated in both the private as well as public sectors in Ireland.

### *Data Issues*

Finally, there is a clear need to modernize the data infrastructure, to allow for advances in artificial intelligence (AI) and machine learning to bring further increases in access and retention to clinical trials. We will address this issue here.

## **Changing Clinical Trials in Ireland**

Of crucial importance to the issues discussed in the previous section, a significant barrier to clinical trial participation in Ireland is the lack of patient access to digitized personal health records and control over their own medical data. Patients should have access to their medical records and be able to move from one treatment center to another and to obtain access to trials. This is particularly important for patients with rare diseases, who may need to travel outside their local area to access the best treatments and trials.

A suitably designed digital platform can provide a solution to this problem by allowing patients to access their personal medical records and connect with their healthcare providers to learn about new treatments and clinical trials. Such a platform enables real-time (real-world)

monitoring of patients' conditions, which can help patients and healthcare providers make more informed decisions about treatment options. Furthermore, this platform's digital asset management system encourages long-term patient participation in trials, providing opportunities for healthcare providers to extend their reach and increase their revenue through research and clinical trial involvement. In short, such a platform is designed to unify health and research to advance both knowledge areas.

There are good clinical reasons to promote this kind of activity. Evidence suggests that being treated in a center where trials are offered is associated with better patient outcomes. Patients who are treated at centers with clinical trials have access to the latest treatments and technologies, which can improve their health outcomes. Better outcomes lead to better value to the overall health sector. Therefore, improving access to clinical trials in Ireland is critical for improving the quality and value of care provided to Irish patients.

Increasing the quality of the health interventions through clinical trials improves patients' outcomes. Improved outcomes lead to improved value to the overall system. Improved value through clinical trials leverages the substantial foreign direct investment incoming to Ireland through the pharmaceutical and med-tech investments.

For these reasons and more, the clinical research enterprise should focus on patient-centered solutions that encourage patients to connect with their healthcare providers, allowing them access to information about new treatments and clinical trials and real-time monitoring of their conditions. Such access is particularly beneficial for those who may not have been previously aware that participation in clinical trials was a viable option, or who had yet to be invited by their healthcare providers into opportunities to benefit from state-of-the-art treatments.

### **Real-World Evidence Driving Quality and Value in Healthcare**

The kind of platform we have been discussing further collects data in a digital health and research data "lake" that is used for post-market surveillance of medical products to improve patient outcomes even more, and to increase the overall quality of the healthcare delivered in Ireland. As new treatments are used in the country, payers can track the longer term effects of these interventions, to ensure only the best treatments continue to receive financial support.

As the platform grows and continues to incentivize patient participation, it can help bridge the gap between high-performing healthcare systems in Europe and their counterparts in America and Asia, allowing patients access to ground-breaking treatments and creating improved health outcomes for all. This amplifies the return on investment Ireland derives from the substantial foreign direct investment from pharmaceutical and med-tech sectors and provides a much-needed solution to the problems posed by a lack of European access to clinical trials. This is truly the time for a change, and Ireland can rise in the forefront meeting these challenges.

## **Conclusion**

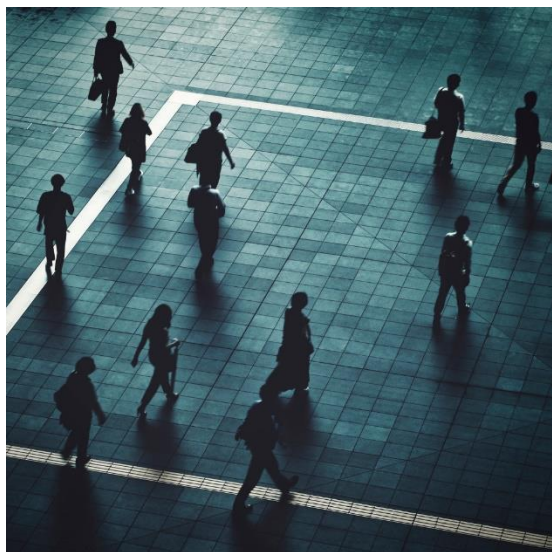
Increasing clinical trials activity in Ireland is a healthcare priority. Direct benefits include improved outcomes and value for the patients and the healthcare system. Byproducts come in the form of increase in return on foreign direct investment for Ireland. Improvements in digital health platforms including AI and machine learning can help drive this important change.



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## Going Beyond the Guidance: Getting Business Benefit from Change Management

Michelle Anastasi



Change management is integral to ensuring appropriate implementation and maintenance practices for pharmaceutical quality systems (PQS).

Effective change management systems ensure that innovation and continual improvement are facilitated, that change is appropriate and proportionate, and that key personnel take a level of ownership of the change. Processes related to change management must include an understanding of the current state and a vision for the future state.

### Change (Mis)management

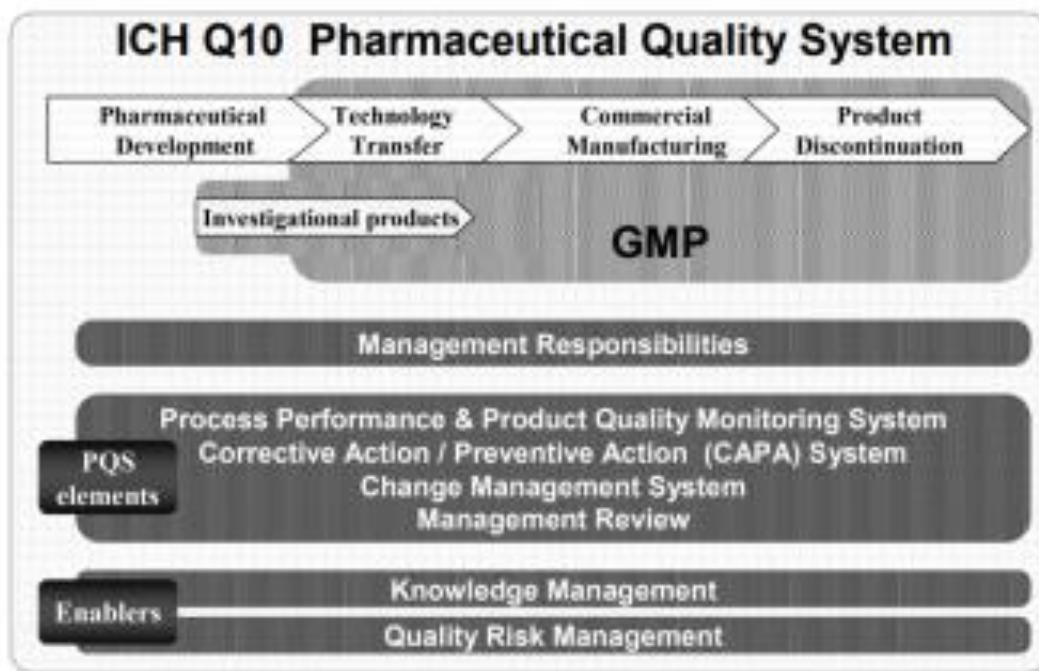
The challenge, however, is that people and organizations both resist and embrace change, and far too frequently the process fails to deliver against the required objectives. How change is communicated and managed will play a pivotal role in determining whether success or failure is the dominating outcome for a business.

### An International Framework for Pharmaceutical Quality Systems

The International Council for Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guideline Q10 describes a comprehensive framework for a PQS. The ICH Q10 system does not add requirements beyond existing regulatory compliances; rather it standardizes the framework to that of the International Organization for Standardization

(ISO) and works with regional Good Manufacturing Practice (GMP) regulations. This standardization ensures global alignment—ultimately saving significant time and any potential reworking when expanding the geographic reach of a product.

Diagram of the ICH Q10 Pharmaceutical Quality System Model



The ICH Q10 and the U.S. Food and Drug Administration (FDA) guidance that supports its implementation assists companies to find a standardized approach and adopt a more comprehensive and holistic way of evaluating the risk that any change might pose.

The process should be defined and documented, and all key functional areas and personnel identified. A structured framework such as the ICH Q10 ensures consistent assessments without gaps are used to inform decisions and to evaluate change. For example, a manufacturing process change can be evaluated using the same structure as a label change. Although some aspects and details will not be applicable to all stages and scenarios, the overarching process of the assessment and moving through the decision-making should be structured in the same way.

## **Working Through the Change Management Process**

Having a well-structured change management system, including procedures that detail how and when to proceed and how to evaluate change, is critical to ensuring that the quality and commercial viability of the product is not compromised.

In the current state, for example where a manufacturing process is already under way, there are likely to be specific details contained in the marketing authorization. An evaluation of the current state and the future state will involve detailing and prioritizing all the elements that must be modified, or may be optional but desirable, to get to the future state. Often companies start to get a little tripped up in that process, because there are a lot of complexities within that change state. Functional heads can lose sight of the broader impact, for example, on how a change might impact whether the product can be distributed in another market.

Having a defined process for working through change and going through an assessment process of which functional heads need to be involved in thinking through the change, how that affects other processes, and how that change should be documented is key to good change management. Again, the ICH Q10 assists the process of working across different areas of expertise and within varying jurisdictions and countries by ensuring the documented process and requirements are developed in a standardized, accessible way and in a known sequence. It is clear to all personnel what the requirements are in managing and documenting changes and the filings that are required for the various marketing authorities.

During manufacturing, for example, change management would consider a change in the context of the impact to the facility where the equipment is used, the validated state of both the equipment and the process, the impact to testing, the impact to all documentation involved (such as test methods, forms, batch records, calibration, maintenance forms and plans, and regulatory filing) and would detail a plan for implementation considering each of these changes and the relative timeline and dependencies of changes in the critical path.

## **Inclusion of Stakeholders**

Consultation with key personnel early in the change process, with a genuine invitation for their input, is integral to their ongoing engagement and the ultimate success of the process overall. The identified stakeholders will generally be from, at a minimum, technical operations and engineering, regulatory affairs, and quality assurance (QA), and must fully evaluate the proposal from their functional point of view. For example, regulatory affairs should always evaluate the impacts on regulatory filings, while QA should evaluate all changes and oversee the entire change management process.

This would include the identification of the systems, processes, and documents that would most likely be impacted by the proposed change. They may also be able to flag any concerns and they would have knowledge that the proposer of the change may lack. They should approve any changes before starting the change process and have the power to modify or reject the change.

Many companies employ a Change Control Review Board to consider these impact assessments and ensure each department is considering the change from all perspectives.

The Change Control Review Board is a set of individuals, functionally specific to the change. QA and regulatory affairs would typically be standing members to ensure an overarching perspective and ongoing compliance with regulatory requirements, respectively. Smaller businesses may not need an entire formal Change Control Review Board, but they must ensure they have oversight of any changes, particularly when outsourcing manufacturing, and of the resulting effect on quality and regulatory requirements.

## **Quality Risk Management and the Marketing Authorization**

Integral to any change management process is the inclusion of quality risk management. The ICH Q10 assists companies to evaluate risk with a standardized approach. The evaluation and understanding of risks apply to each individual component, each functional area, and the overall



process and product. This is, in theory, straightforward, but may rapidly become complex in execution, so a defined structure for managing and evaluating changes is essential.

The marketing authorization includes details of production, incorporating location, manufacture, testing, packaging, logistics, and distribution of the product. Modifications to any of these requires a detailed evaluation of the change and the impact, or potential impact, of that change on product quality and patient safety.

For example, if there is an increased risk of failure to supply to meet patient demand, the risk is proportional to the product. A single-manufacturer, life-saving medication carries a much higher patient risk than a generic, multi-producer headache tablet.

### **Key Steps for Evaluating Change Objectives**

Any change management process should encompass an evaluation process to ensure objectives were met. Having an effectiveness check with relevant metrics provides an understanding of the business benefit of the implemented change, as well as any positive impact on the quality and safety of the product.

A simple example might be a manufacturing change to increase product yield. The introduction of a larger machine may double the apparent number of tablets produced for each hour worked, but downtime for maintenance may increase. The assessment would need to consider whether, over a predetermined timeframe, the new machine genuinely increased productivity or, once all factors were taken into account, there was a non-significant improvement or even a decline. Did the cost of the change justify the expense? The objective for the change must be fully assessed against the initial proposal for change and costs at all levels should be determined to provide a complete economic analysis.

### **Inside the Business to the Global Marketplace**

Good change management involves a detailed procedure, detailed documentation, and open functional discussions that allow a company to assess the impact of the change on a technical and business level.

The ICH Q10 structure enables internal clarity of management and assessment processes for change, plus greater standardization to support access to international markets via a known framework that supports heavily regulated processes.



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FORM & FUNCTION

## **Closing Pharma's Financial Chasm by Measuring and Improving Development Velocity**

Donna Conroy, MS



In the December 2022 issue of *Clinical Researcher*, I penned an [article](#) introducing the concept of Development Velocity (DV), the speed at which a pharmaceutical company moves a new drug through the development process. In the months since, new information has emerged on the widening financial chasm pharma is facing on two fronts: increasing development costs and diminishing market exclusivity.

Together, these challenges validate the need for pharma to improve DV or face difficult decisions about reducing research and development (R&D) expenditures; decisions with life-altering implications for patients.

Strategic end-to-end drug development, a lesser-known component of the R&D process that occurs in parallel with clinical trials, represents a major opportunity for pharma to recoup costs and find critical time efficiencies. By measuring and improving DV in this untapped area of R&D, pharma can begin closing the financial chasm.

Our research found that adopting technology to increase DV with data integration and workflow automation tools alone can save tier-one pharma companies an average of \$202 million and 212,000 person hours annually. DV's purpose is to get drugs to market faster. Earlier revenue streams are beneficial and can create competitive advantages that help drugs win “first to market” status and benefit from the additional and well-documented 6% market share [advantage](#).

### **Pharma's Expanding Financial Chasm**

Deloitte recently reported the average [cost](#) to develop a new asset climbed to a staggering \$2.2 billion in 2022, an increase of \$298 million from 2021. Further, the top 10 drugs that lost market exclusivity in 2022 together generated \$17 billion in [yearly](#) sales.

Refilling the pipeline is becoming increasingly challenging, as macroeconomic changes impacting deal flow are starting to have downstream implications—such as fewer acquisitions of innovative products. These factors create a feedback loop where existing drug development programs are under ever-increasing pressure to move faster to help offset lost revenue and rapidly rising costs.

When we drill down, the financial benefits of accelerating development become clear. Tier-one pharma companies (see chart), defined as those with high annual revenue (>\$20 billion) and high commitment to R&D (>15%), saw combined annual revenue of \$687 billion in 2022, with an average 18% of revenue, or \$126 billion, dedicated to R&D efforts. Our research found these companies collectively spent an estimated \$2.8 billion just on data analytics to support strategic end-to-end development efforts (range \$69 million to \$359 million per company; average \$201 million) in 2022.

Introducing comprehensive artificial intelligence (AI) technology into this R&D component can reduce data analytics costs by 67% or \$1.9 billion (range \$58 million to \$251 million per company; average \$135 million) by eliminating inefficiencies such as redundant analytics, slow and manual analytics, and siloed analytical technologies. Factor in additional savings from project management efficiencies like aligning data findings to specific tasks, sharing information, and linking interdependencies, and the cost savings increase significantly.

The benefits transcend both ends of pharma’s ledger, with earlier revenue generated from drugs that get to market faster and the potential to tap into the 6% first-to-market advantage. Together, these factors help pharma close the financial chasm.

<b>Tier-One Pharma Companies: High Annual Revenue (&gt;\$20B) &amp; High Commitment to R&amp;D (&gt;15%)</b>			
<b>Company</b>	<b>2022 Annual Revenue (\$B)</b>	<b>2022 R&amp;D Spend</b>	<b>R&amp;D % of Revenue</b>
Roche	\$ 63.281	\$ 16.023	25%
Eli Lilly	\$ 28.541	\$ 7.191	25%
Merck	\$ 59.283	\$ 13.548	23%
AstraZeneca	\$ 44.351	\$ 9.762	22%
BMS	\$ 46.159	\$ 9.509	21%
Boehringer Ingelheim Corp	\$ 26.380	\$ 5.510	21%
Novartis	\$ 51.828	\$ 9.996	19%
GSK	\$ 36.720	\$ 6.870	19%
Gilead	\$ 27.281	\$ 4.977	18%
Amgen	\$ 26.323	\$ 4.434	17%
Johnson & Johnson	\$ 94.943	\$ 15.386	16%
Takeda	\$ 31.764	\$ 4.682	15%
Sanofi	\$ 49.500	\$ 6.706	15%
Pfizer	\$ 100.330	\$ 11.428	11%*
<b>TOTALS</b>	<b>\$ 686.684</b>	<b>\$ 126.022</b>	<b>18%</b>
Annual revenue sourced from Yahoo Finance as of 5/11/23			
BI, GSK, Sanofi, and Takeda converted to USD based on exchange rates on Google 5/11/23			
*Anomaly due to higher than normal annual revenue due to COVID product sales. 2021 R&D % of revenue = 17%			

### **Pharma’s Financial Chasm Impacts Patients, Too**

The impact of this growing financial chasm may affect healthcare in general. With costs to develop new therapies increasing and market exclusivity decreasing, overall return on investment (ROI) is lower. Shrinking ROI may force pharma to reduce R&D budgets, resulting in less availability of new therapies or fewer studies in expanded patient populations. Our early analysis shows a slight drop in R&D investment in 2022 (currently 18%; down from 19% in 2021), however more data and time are needed to fully evaluate if this is due to shrinking ROI or factors

related to the COVID-19 pandemic (as was the case for the Pfizer anomaly seen in the chart above). This is a trend we are tracking.

## **DV Measures an Untapped Value Opportunity Within R&D**

Strategic end-to-end drug development refers to the cross-functional work required to move a drug to market—work that takes place *after* drug discovery and *outside* clinical trials. Despite investing billions in AI technology to enhance drug discovery and clinical trials, strategic end-to-end drug development remains untapped with no comprehensive innovation; it is laden with manual and siloed legacy processes. The lack of comprehensive data integration and workflow automation tools creates inefficiencies that slow the development journey and increase costs.

While most pharma companies apply *some* internal key performance indicators to measure efficiencies within strategic end-to-end development, the depth and breadth vary wildly. It is important for DV to be adopted as an industry-wide, third-party, mission-critical metric. The main benefit being that DV is a standardized process that normalizes data across drug programs, both within a company and industry wide. Situational components and variables, large and small, are accounted for among development programs. DV considers factors such as disease size, available datasets, team size, and funding, to name a few.

The DV Index score is similar to a FICO score: it assigns different weights to variables that impact performance. In the FICO example, the credit rating of a college student is normalized to provide a score that can be accurately compared to a long-time homeowner with established credit. By normalizing data in similar fashion, a rare disease and cardiovascular disease can be evaluated on an equal plane, despite rare diseases typically involving significantly less data and smaller teams. DV accounts for these anomalies in its scoring methodology to provide a uniform measure of time and cost efficiencies across drug development programs.

## **DV = Efficiency + Time**

DV utilizes a proprietary formula that provides an impartial and unique assessment of a drug development program's comprehensive operational efficiency. While current drug development

efficiency models only consider the financial efficiencies, DV measures both financial efficiencies (i.e., cost savings) and time to market.

Time to market is significantly impacted by the hours it takes to accomplish more than 300 required tasks in a product's development roadmap. Inefficiencies and redundancies result in hours wasted by pharma and its vendors. In 2022, our research found tier-one pharma companies collectively spent an estimated 3 million hours on data analytics alone (range 75,000 to 391,000 hours per company; average 212,000 hours) for various roadmap tasks in different development phases of their pipeline programs.

With comprehensive, cross-functional technology, pharma could have completed those same data analytics in 117,000 hours. In other words, in 2022 alone, pharma collectively wasted 2.9 million hours (range 72,000 to 329,000 hours per company; average reduction 203,000 hours). Assessing a drug program's velocity is a critical component of DV. Reclaiming time helps accelerate therapies to market while closing the financial chasm.

DV measures more than 200 critical factors that foster inefficiencies. They fall into three primary categories:

***Data Utility: How science is used for decision making***

Example: Redundant literature searches among cross-functional teams

Time Inefficiency: The same base of data from 50 publications was used to answer questions across teams. Data findings were not shared across teams, resulting in redundant work hours.

Cost Inefficiency: Vendors typically charge between \$50,000 and \$250,000 to conduct literature searches. Multiple charges were made to identify and analyze the same datasets.

***Project Management: Effectiveness in orchestrating cross-functional teams and tasks***

Example: Lack of collaborative tools limits the sharing of interdependent deliverables

Time Inefficiency: Hunting for documents that inform workflow, whether on SharePoint or directly from a colleague, is time-consuming.

Cost Inefficiency: Multiple technology purchases to accommodate the needs of individual functions.

***Corporate Approach: The role of corporate culture in strategic development***

Example: Inability to pivot a strategy quickly when competitive data releases.

Time Inefficiency: Without keeping everyone up to date in real time, the process for quick cross functional decision making is laden with multiple steps.

Cost Inefficiency: Time to market is threatened and may impact overall revenue.

The impact of inefficiencies varies; some slow development by only a few hours or days, while others derail progress for weeks or months. However, in a multi-year drug development program, even seemingly minor inefficiencies compound over time to slow development timelines and increase budgets.

Inefficiencies, once identified, ranked, and scored, must be reduced or removed for meaningful change to occur. Our industry must overhaul the strategic end-to-end development process and utilize emerging technology and tools built specifically to address the needs of cross-functional drug development teams. Replacing antiquated processes with AI technology to improve data integration and workflow automation will accelerate strategic development and provide a resource to begin closing the financial chasm.

**Conclusion: Why Focus on Efficiency in Drug Development?**

Drug development is expensive and time-consuming, but it is possible to create efficiencies that offset the financial chasm of increasing costs and diminishing market exclusivity currently impacting pharma. By focusing on improving DV and incorporating AI technology into strategic end-to-end drug development, every pharma company can create game-changing efficiencies in R&D.



Committing to innovation will open the doors to urgently needed cost and time savings in an era when pharma faces unprecedented fiscal pressures. Patient lives are at stake and strategic drug development offers an untapped solution to drive innovation in R&D, one that allows teams to fail fast or succeed fast. The time to embrace innovation in drug development is now.

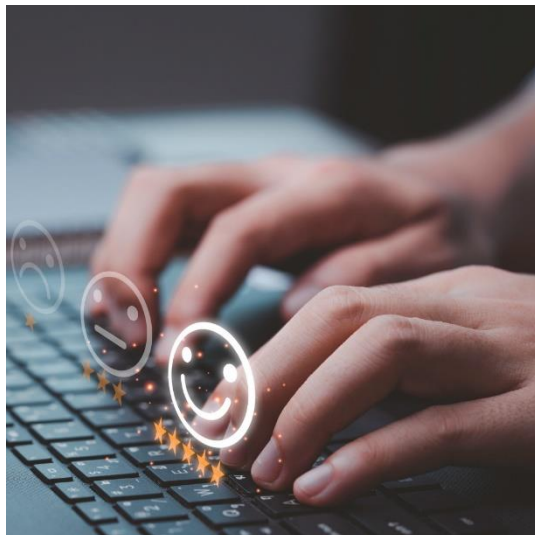


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**ON THE JOB**

**CRA Soft Skills for Pre-Study Evaluation Visits**

Elizabeth Weeks-Rowe, LVN, CCRA



The pre-study evaluation visit is far more than a clinical research associate (CRA) confirming an investigational site’s facilities, equipment, and personnel for potential study participation. The pre-study evaluation visit is the impetus for relationship development/sustainability with the investigational site, and if conducted appropriately, builds the framework for the collaborative relationship integral to study conduct. The CRA is an extension of the study sponsor, and his or her behavior bears the

weight of this representation. The CRA must therefore cultivate a positive impression at the beginning of the evaluation visit process; the resulting outcome will influence site selection, site willingness to participate, and future endeavors. It must be navigated carefully.

**Making the First Impression Count**

First impressions are multifaceted, fluid; they lay the groundwork for a growing, more mature impression that builds to the current impression and onward to a lasting impression, whether positive or negative. A successful impression is borne of professionalism, supported by preparation, and should be framed with positivity for the outcome desired.

There are specific behaviors, when demonstrated by the CRA during the pre-study evaluation visit, which will elevate visit conduct and ensure a positive impression with the investigational site. For example, the CRA should:

- Be flexible when scheduling the pre-study evaluation visit with the site. The CRA is scheduling for one, whereas the site representative is scheduling for multiple participants/departments and has less flexibility. Successful accommodation requires compromise.
- E-mail the study coordinator a list of questions to be asked ahead of the visit. This helps the site to better prepare for the visit, and the CRA may even receive answers to some questions before the visit. This facilitates effective time management and support for all participants.
- Provide an agenda that delineates activities, required attendees, and timeframe. This provides the site with the parameters to organize personnel and logistics effectively.
- Provide the principal investigator (PI) and site personnel with the protocol, slides, and all documents to be reviewed/completed in advance of the visit.
- Obtain the correct address and directions to the investigational site from the study coordinator/site representative, instead of relying on an address in a database that may be incorrect.
- Print a copy of the slides and protocol to bring to the visit and provide for any attendees who want to write notes during the presentation. Obviously, the site can print copies, but this is sometimes forgotten in the rush to organize things. It is helpful to a site if the CRA does this. Alternatively, if there is an equipment or internet failure, printed copies ensure the visit can proceed when there is no other option for review of information.
- Bring the schedule of assessments from the protocol to the visit, as it provides a large-scale view of protocol activities and helps the site further consider its capabilities (visit frequency, patient burden, timing, resources).
- Arrive at the site 15 to 20 minutes before the visit. Punctuality demonstrates respect for others' time and the CRA's efficiency, and gives the CRA extra time to set up.
- Be very familiar with presentation content and mindful of presentation timing, due to unanticipated or unavoidable schedule changes by site staff. At the pre-study evaluation visit, the CRA should confirm how long the PI is available in person and adapt accordingly. For example, if the PI's availability changes from 60 minutes to 20 minutes, the CRA can pivot and only review the most critical required information to fulfill visit requirements.

## **Other Courtesies and Considerations**

If the PI is unexpectedly not able to attend the pre-study evaluation visit, the CRA should not automatically reschedule the visit. The CRA may be able to schedule a teleconference with the PI to review protocol and required information soon after the pre-study evaluation visit, while still completing the onsite evaluation visit with the remaining site members. This will prevent revenue loss associated with changing travel and schedules. The CRA must obtain permission from study management to follow the aforementioned process.

During the protocol presentation, the CRA should stick to the critical points and let the bullet points guide discussions and supplement attendees with information. It is not necessary to review every bullet point and every slide in the presentation, and the audience will appreciate this effort.

The CRA should be professional, respectful, and kind to site staff. They are graciously allowing an “outsider” into their facility and committing a large amount of time for study consideration.

The CRA should be clear on the questions to ask and the information to present. Lack of preparation will hinder what should be an efficient and equitable process.

The CRA should understand that the pre-study visit is a reciprocal consideration. The site personnel are assessing the CRA as much as the CRA is assessing them. If the CRA is informative, patient, and positive, it will result in transparent and professional dialogue that illuminates and engages all players.

The CRA should give positive feedback. If the study coordinator was responsive and fulfilled all advance requests to organize the visit effectively, make sure to thank the study coordinator and inform the PI of the study coordinator’s effort. If the PI was generous with his/her time, thank them sincerely; the investigator’s time is very limited and this investment shows their high regard for the study/contract research organization/sponsor.

## Conclusion

Hardworking site personnel deserve recognition and respect, for they are in the proverbial trenches executing study activities and preserving the tenets of patient safety and credible data that are the framework for the clinical trials we conduct.



**Elizabeth Weeks-Rowe, LVN, CCRA,** ([elizabethwrowe@gmail.com](mailto:elizabethwrowe@gmail.com)) is an independent research consultant and former clinical research coordinator with a track record of expertise in site selection and education for the contract research organization industry. She last wrote for *Clinical Researcher* in October 2022 (“[Lessons from Female Innovators in Clinical Research](#)”).

PRESCRIPTIONS FOR BUSINESS

## How Social Determinants of Health Affect Clinical Trials and What eClinical Solutions Can Do to Help Level the Playing Field

Wessam Sonbol, CSM, CSPO, ICP-ACC



Thanks to social media platforms and their ability to widely disseminate information, whether fact or fiction, we live in a society where words and terms “go viral” almost as fast as video clips do. We are often inundated with terms like “diversity,” “equity,” “inclusion,” and “social determinants of health.” These particular words and terms are more than just descriptors though—they are necessary to acknowledge and accept in order to progressively move our field forward. Harvard is even offering [a class](#) on the subject!

Mission-driven companies that offer eClinical and digital healthcare solutions know that using technological advancements in order to provide access to more patients—effectively closing the inequality gap—is necessary for the betterment of the clinical research field at large.

[The U.S. Department of Health and Human Services](#) (HHS) states that the “social determinants of health (SDOH) are the conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks.”

According to HHS information tied to its Healthy People 2030 initiative, SDOH can be grouped into five categories:

- Economic Stability
- Education Access and Quality
- Healthcare Access and Quality
- Neighborhood and Built Environment
- Social and Community Context

Basically, SDOH are social and economic factors that influence the health and well-being of individuals and their local communities. These factors are shaped by the distribution of money, power, and resources—impacting a patient’s access to quality healthcare and therefore having a significant impact on their health outcomes.

[The World Health Organization \(WHO\)](#) defines “social determinants of health equity” similarly as “the conditions in which people are born, grow, live, work, and age.” These conditions, again, include factors such as education, employment, housing, access to healthy food, transportation, exposure to stressors and violence, and access to healthcare and social support networks. SDOH are also influenced by broader social factors such as racism, discrimination, and poverty—hence the addition of the word “equity.”

**DELVE** HEALTH

## What are SDOH?

Read our latest blog about how SDOH have **significant impacts** on a patient's access to quality healthcare—and what Delve Health is doing to be a part of the solution.

[LEARN MORE](#)

[www.delvehealth.com](http://www.delvehealth.com) | [contact@delvehealth.com](mailto:contact@delvehealth.com)

**Social Determinants of Health**

- Education Access and Quality
- Health Care Access and Quality
- Neighborhood and Built Environment
- Social and Community Context
- Economic Stability

## The Many Pain Points of SDOH

The impact of SDOH on a single patient's health and healthcare access is *significant*. For example, research has shown that people who live in poverty are more likely to experience more serious health outcomes such as chronic diseases, mental health disorders, and premature death. Similarly, people who experience discrimination based on their race, ethnicity, or gender are more likely to experience negative health outcomes. For example:

- People with lower incomes have a higher risk of chronic diseases such as diabetes and heart disease.
- Individuals who live in neighborhoods with limited access to healthy food (e.g., “[food deserts](#)”) are more likely to have poor nutrition and suffer from obesity.
- Lack of access to quality education can result in reduced economic opportunities and contribute to poor health outcomes.
- Unhoused citizens face significant health challenges, including chronic diseases, mental illness, and substance abuse.
- Racism and discrimination can lead to poor health outcomes for marginalized groups, including higher rates of chronic disease and mental health disorders.

SDOH also have adverse influence on the utilization and costs of care. People who experience social and economic disadvantages are more likely to have severely limited access to healthcare services, which can lead to delayed diagnoses, untreated illnesses, and increased healthcare costs over time ([see: Health Equity Tracker](#)). Therefore, SDOH can also have a significant impact on the design, implementation, and outcomes of clinical studies; for example, through their influences on these mechanisms:

- **Recruitment:** SDOH can affect efforts to recruit study participants, as individuals from low-income households and/or limited education may be less likely to participate in clinical trials due to transportation or time constraints; mistrust of doctors and other healthcare professionals; or a lack of awareness of their eligibility.



- **Retention:** Participants from marginalized or underrepresented populations may face social and economic barriers that make it challenging to complete clinical trials, such as competing responsibilities or lack of social support networks.
- **Data collection:** SDOH can impact the quality and completeness of data collected during clinical research. For example, a patient’s socioeconomic status may affect his or her ability to provide accurate medical history or access to healthcare resources that could affect the interpretation of clinical outcomes.
- **Intervention effectiveness:** SDOH can impact the effectiveness of interventions evaluated in clinical research. For example, social and economic factors such as housing conditions, access to healthy food, and social support networks can impact and individual’s ability to adhere to treatment or achieve positive health outcomes.

### **Putting eClinical on the Case**

Considering all of the factors listed above, it is crucial for clinical study teams to address the realities of SDOH when designing and conducting trials. This can include integrating eClinical technology platforms and solutions to assist in executing strategies to recruit and retain diverse study populations, passively collecting patient data, and incorporating interventions (such as “nudging” patients to complete their eDiaries) to ensure patient compliance.

Digital healthcare providers can help address SDOH by leveraging the technology solutions they create to applaud and support the strides regulatory bodies and international governmental agencies are making to bring equitable, quality access to healthcare and clinical trials worldwide. Additionally, we must also work to provide the solutions to these complex challenges ourselves. Here are some ways digital healthcare platforms can help:

- Telemedicine can provide patients in remote or underserved areas with access to quality healthcare providers of their choice.
- Digital health and eClinical study apps and wearable devices can help patients manage chronic conditions such as diabetes and hypertension.
- Virtual healthcare platforms can improve mental health access for individuals in need of behavioral healthcare services.

- Health information technology can improve care coordination and help healthcare providers better manage patient care.
- Digital tools can be used to promote health education and awareness, such as healthy eating and physical activity.

Further, eClinical solutions can support virtual, hybrid, and decentralized clinical trials worldwide. Remote patient monitoring via wearables, biosensors, other medical devices, telehealth visits, and communications via SMS or other messaging apps remove barriers such as costs to travel to a site and a clinical trial being inaccessible due to geographical locations.

### **The Big Picture**

Virtual clinical trials and digital healthcare are the future of real-world solutions for many of the woes facing the clinical research enterprise. Technology platforms help to close the gap in equity and bring quality healthcare and equal opportunities to participate in clinical trials—saving patient lives.

In addition to helping patients feel empowered to take charge of their own health, digital and wearable technology solutions benefit the clinical research industry and healthcare overall. Improving the gathering of quality data and increasing diversity within the patient participant population will lead to more accurate and representative data within clinical studies—eventually impacting drug therapies, treatment protocols, and healthcare at large.

To reiterate, SDOH play a significant role in health outcomes. They are an important and often overlooked aspect of a patient’s health and well-being. Acknowledging these challenges and barriers to fair and equitable access to quality healthcare, and therefore the potential recruitment into a clinical trial, is just the first step. Understanding and addressing these factors are *crucial* for improving patient-reported outcomes and reducing the operational costs to successfully complete a clinical study.

It is imperative that eClinical solutions and digital healthcare providers work together to close the equity gap. This is not only beneficial to all patients around the world, but it is constructive for the clinical research enterprise as well. Reaching out to and recruiting more diverse and

underrepresented patient populations to participate in clinical trials is valuable in that leads to diversified, real-world data and therefore real-world evidence about how, for example, a chronic disease might present itself differently in various populations. Analyzing wide-ranging data leads to learning more about our patients around the world—how different treatment plans and drug therapies can be applied to distinct patient profiles, hopefully leading to improved treatments and therapies for a healthier global population.

## **Conclusion**

Aside from the benefits to general healthcare and to our specific field of clinical research, focusing on SDOH is *simply the right thing to do*. By focusing on these challenges and using innovative technology platforms and wearable devices to address them, we can create a more equitable and just healthcare system, with better access to clinical trials, that promotes *health for all patients—worldwide*.



**Wessam Sonbol, CSM, CSPO, ICP-ACC**, is Co-founder and CEO of [Delve Health](#) in Golden Valley, Minn., and has 20 years of experience in Phase I–IV, Investigational Device Exemption, and 510(K) clinical research business operations.

RECRUITMENT & RETENTION

## How Sponsors Can Support Sites with Data Analytics to Meet New Trial Diversity Regulations

Rohit Nambisan, MS, MA



Clinical trial participation amongst minority groups in the U.S. is woefully inadequate—a challenge that has plagued this industry for years. In December 2022, substantive diversity, equity, and inclusion (DEI) [legislation was signed into U.S. law](#) and went into effect in February 2023 to help correct the significant disparity and hold sponsors responsible for ensuring that their trials represent diverse patient participant populations.

No one doubts the inherent value of broader representation in clinical trials; however, sites are burdened with delivering DEI enrollment requirements. Without an effective strategy, such regulation might impact the ability to carry out any research at all, according to conversations with industry research professionals.

“Everyone realizes the benefits of representative populations as participants in clinical trials,” said a clinical operations executive at a multinational pharmaceutical company in an April 2023 interview. “Now the issue has more to do with how granular regulations might get, how it fits into overall drug development strategies, and whether it might ultimately hinder our ability to address the requirements across all regions of development while controlling for costs and ensuring scientific rigor.”

While sites are responsible for participant enrollment, now sponsors must actively provide diversity guidance and support during protocol design and study start-up. Sponsors will need a reliable mechanism to ensure a diverse representation of participants in their trials or risk derailment.

### **Supporting Sites with Data Analytics**

One way to mitigate potential impacts is for sponsors to enable their site partners with systematic data analytics. Sponsors and contract research organizations (CROs) need to manage ever-growing volumes of data in real time to ensure that trials meet planned timelines while addressing the diversity plans they have submitted to the U.S. Food and Drug Administration (FDA). Yet managing such data is difficult across all stakeholders, particularly given the rapidly expanding and disparate array of trial data sources out there.

[According to a 2021 study by Tufts University](#), Phase III clinical trials generated an average of 3.6 million datapoints, or three times the amount of data collected by late-stage trials in 2011. Lokavant's internal analysis suggests that by 2030 these clinical trial datasets will skyrocket to seven times that of 2011.

Today's avalanche of data is both a blessing and a curse. Data are only useful if they can be analyzed effectively across all teams, which grows more challenging due to novel data types and increasing data volume. With the new DEI requirements, data analysis and open communication will become even more important—and more onerous. For small to mid-size biopharma companies, this could be devastating.

Fortunately, advanced data analytics can shift the paradigm in clinical trial operations. Technology that centralizes data sources drives machine learning models that anticipate clinical trial events (and their impact on trial execution) and empowers sponsors to notify sites when they see a risk signal, mitigating challenges before it is too late. Such technology reduces friction with outsourced vendors, improves data transparency, and unifies complex interactions across stakeholders participating in the trial to ensure that each has the right information at the right time, optimizing trial conduct.

When sponsors, CROs, and sites are reviewing the same data, they can make important real-time decisions for the success of their trials, including those involving recruitment to meet enrollment numbers. Toward this end, artificial intelligence (AI)-based platforms are already [proving their value](#). In one case, results revealed a 70x improvement in enrollment forecast accuracy, more than \$1 million in savings from participant retention, and six months' time savings from detecting site noncompliance issues.

“Smart companies are starting to leverage advanced technology and data analytics to better predict the progress of trials,” added the same clinical research professional quoted earlier.

“There’s a huge advantage in being able to leverage robust statistical monitoring to see trends in data and be able to identify trials that might be going off track before it is too late. Ultimately, that will save sponsors a lot of time and money and help align with sites—particularly with DEI initiatives.”

### **Preparing for the Next Frontier**

Diversity challenges are the next frontier for advanced analytics in clinical trials. Data-driven technology gives sponsors and vendors complete, continuous visibility into the progress of planned DEI initiatives. Data-agnostic predictive platforms can generate important insights into, just for example, which sites offer access to diverse and indication-specific participant populations—across a wider set of data sources than have been utilized traditionally.

Where sponsors have historically contracted with the [same, familiar sites](#) so the pool of participant data is, likewise, homogenous, they can instead use these new data-driven insights to engage with a broader range of sites. A system that leverages multiple data sources provides insights that maximize diverse recruitment and minimize bias at the outset of a clinical trial.

In addition, real-time analytics can provide rapid feedback to sites on the diversity of their randomized participants. This empowers sites, which have typically been disenfranchised from study conduct analytics, to make timely adjustments in terms of optimizing recruitment plans in-line with diversity requirements.

## A Call to Action for Sponsors to Share Data Analytic Insights with Sites

Now that the FDA is requiring adherence to diversity plans, it's crucial that sites and sponsors align on and collaborate with trusted analytics. Clinical trial sponsors and CROs have even more to manage, more data to assess, and more risk. Sites have the task of recruiting a representative population for the trial and ensuring its success through the collection of high-quality data. Diligence from stakeholders in all of these roles is critical for expediting novel therapies to patients.

Anticipating when a trial is veering off the established plan for diversity and population representation is critical, and doing so *before* the end of the trial or enrollment period is paramount. If a sponsor can act quickly and notify the site, site managers can pivot and ensure that the trial stays on track to hit all its milestones.

The new DEI requirements in the U.S. represent an important formal step in ensuring that clinical trials reduce outcome bias while producing the information that researchers need to prove that novel therapies are truly safe and efficacious. Now it is up to sponsors to do their part to address disparities that have plagued healthcare, and to empower and collaborate with sites on execution.



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## Data Management Q&A: Stepping Back to Get the Big Picture

Feedback provided by Carly Baker, CCDM, and Alice Wang, MS



**Q: What are the benefits that having an Independent Data Management Committee (IDMC) can introduce when conducting clinical trials?**

**A:** The primary purpose of an IDMC is to protect the safety of trial participants and maintain the integrity of trial data. This can be hugely beneficial to sponsors because it ensures trials of effective interventions have the best chance of success while minimizing the risk to patients from ineffective or unsafe interventions.

IDMC members are usually the only ones to see accumulating, comparative data from a trial. They can make a risk-benefit assessment of the study which leads to recommendations concerning its continuation, modification, or publication. Independent review of interim deliverables also ensures ongoing data cleaning, therefore preventing a data backlog at the end of the trial.

**Q: Have recent trends in clinical trials—such as decentralized trials and remote patient monitoring—changed how the data are managed?**

**A:** Recent trends have led to changes in how data are managed by both the patient and data management.

From a data integrity perspective, there is a need for patient training to prevent errors. With remote trials, the emphasis is very much on the patient to collect data in their own home, and it is key they understand what is expected of them. Practical training should be delivered, with its outcome recorded as part of the trial protocol and design. For example, if participants are using



their smartphone to record data, they need to demonstrate that they have completed and passed training in using that tool before recording their data for a trial.

From a data management perspective, there is a huge amount of data coming in externally (e.g., from wearables, patient diaries, etc.). This means that a lot more primary endpoint data are being collected outside of our traditional electronic data capture system. That brings challenges with regards to how frequently the data are brought in, how much are reviewed, and how we can ensure that the review is adding value to the trial because it is not possible to review all the data. Data review should focus on the primary endpoint and key data, not everything.

Source data are another potential issue. For example, historically, patient diary data would have been recorded in a traditional paper format. In recent years there has been an industry drive to collect these data electronically in order to increase data quality. However, if there is an inconsistency with the diary data, this cannot be queried, as it is a reflection of how the patient was feeling on the day.

**Q: What can clinicians and researchers do to select the most effective form of data for their trial design?**

**A:** Thinking of your patient population is key. So, for example, if you have an aging demographic, then is a smartphone the most appropriate way forward? If you are in a developing country, would the demographic of people with their own smartphone device be the same as other sites? Do the privacy laws of your site country or region (for example, the General Data Protection Regulation [GDPR] in the European Union) impact the type of data you can collect and how they are reported?

One way to help ensure you select the most effective form of data for your trial design is to engage patient advocacy groups from the outset. They can, for example, help you design questionnaires on the type of data collection that would work for your target patient population. This can improve compliance and the quality of end-of-trial data.

Clinicians and researchers should also consider patient convenience and inconvenience when deciding on the most appropriate data to be recorded. If you have a patient who is having to

travel to the site, is there an option which enables him or her to contribute data closer to home? Again, this will likely increase patient compliance and improve the overall trial data.

**Q: How can historical data and metadata be used to predict future results?**

**A:** Historical data and metadata have been instrumental in retrospective cohort studies and epidemiology. Many research studies use patient demographic data and clinical characteristics in addition to data collected from individual patients (from questionnaires, surveys, or clinical trials) to predict trends and hazard ratios for disease progression and overall survival. Other relevant sources of so-called real-world data can include both germline and somatic genetic data (e.g., from next-generation sequencing, single nucleotide polymorphisms, copy number variants, biomarkers), tumor information and tumor registry data (stage, grade, histology), SEER (surveillance epidemiology and end results), insurance data (claims, prescriptions, medications), and electronic health records. The aggregation, harmonization, linkage, storage, cleaning, and maintenance of all these different data types are critical to conducting research. Once collected, the statistical and descriptive analysis of these data can be used to inform patient care best practices, longevity, and efficacy of treatments, in addition to lifestyle modifications.

**Q: Why is data visualization important, and how can it effectively be carried out?**

**A:** Data visualization is important when you have large volumes of varied data, and you want to look at trends or aggregate the data. Interactive visualizations through apps and dashboards are becoming increasingly important tools to utilize as we see an increased variety of clinical data sources and types across multiple trial sites.

Crucially, visualizations are interactive. They might start off as a very pictorial representation, but if you want to know more detail on, for instance, a site or subject causing an issue, you can click down into a specific datapoint. Visualizations can enable you to look not just at local outliers, but also to proactively investigate trends within sites to potentially identify fraud or duplicate subjects and protect data integrity. If you were using traditional listings, it would be very difficult to identify those types of issues.

Visualization allows individuals to spend more time gaining a deep understanding of the data and addressing anomalies, and less time trying to analyze data in suboptimal formats.

To effectively carry out visualization, systems need to have capacity to repeat processes routinely and reproducibly to ensure those who need it have access to real-time data for effective decision-making. Our company's desire to facilitate the use of visualization and analytical tools for regulated studies is why we acquired S-Cubed ApS, a specialist biometrics and data visualization company, earlier this year.

**Q: How might this change in regard to differing international approaches to GDPR?**

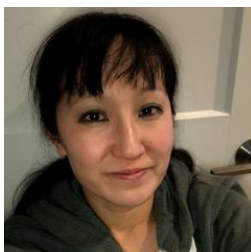
**A:** Because data visualizations may be linked to other released information and used to identify study participants, their creation may be prohibited. GDPR calls for data anonymization, which ensures an individual's personal data cannot be reconstructed and used. While potentially reducing the risk of breaching participant confidentiality, this also represents a barrier to greater understanding of data and, therefore, to more effective governance.

One way to tackle this potential conflict is to use anonymization techniques. These can generate privacy-preserving visualizations which retain the statistical properties of the underlying data while still adhering to GDPR and other strict data regulations. Methods might include the *k*-anonymization process, probabilistic anonymization, or deterministic anonymization, each of which has its own strengths and weaknesses.

This is not just a legal requirement, but an ethical one—participants should have confidence that their privacy will be respected. Agreeing on a framework for mitigating the data risk associated with visualizations should be seen as a shared responsibility between both data custodians and data analysts.



**Carly Baker, CCDM**, is Director of Clinical Data Operations for [Phastar](#).

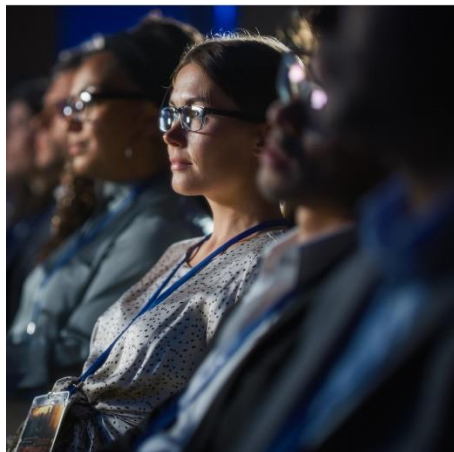


**Alice Wang, MS**, is Principal Data Scientist for Phastar.

SITES & SPONSORS

**Focus Investigator Trainings to Make the Most of Decentralized Clinical Trials**

Marc Crawford, MBA



Decentralized clinical trials (DCTs) are an effective means of reaching more diverse patient populations, overcoming geographic barriers to participation, and reducing day-to-day workload for trial investigators. However, DCTs also pose unique challenges because the critical elements of the trial, from administering treatment to recording and verifying data, no longer take place under the watchful eye of the investigator.

An article posted by the [Association of Clinical Research Professionals](#) notes, “The popularity of DCTs is making oversight of investigators more critical. As trial operations spread and become more remote, the role of the investigator as a center of gravity becomes increasingly vital.” It’s also increasingly vital, then, that the investigator at the center is correctly trained and prepared for all the specific elements of the DCT.

In the case of DCTs, investigator training takes place as investigators continue to join the trial, spreading training out over time rather than accomplishing it all at once, as in centralized studies. Today’s technology provides study sponsors the opportunity to hold in-person, virtual, or hybrid investigator meetings, depending on what works best for them. Regardless of the type of meeting, though, it’s important that all investigators receive clear and consistent training to ensure all sites adhere to the trial protocol.

## **Planning and Training for Success**

The best DCT investigator meeting will have many similarities to the best centralized trial investigator meeting. Sponsors should begin by planning the meeting with the end in mind; that is, prioritize what they need investigators to thoroughly understand by the time the meeting ends and design the content around that. Consider the aspects of the DCT that will be new to investigators accustomed to centralized trials. Be proactive about challenges they may encounter and recommend courses of action. Once clear and carefully considered content has been established, add elements to the meeting that will engage the investigators in ways that not only keep them aware, but reinforce the information being presented.

Because there is a lot of important information being delivered in a text-heavy format, it's helpful if the sponsor visually calls out the most critical details. For example, try to differentiate high-priority presentation slides from those of a lower priority. This could be through something as simple as placing an icon on the slide and telling investigators this is how they'll know this is a slide to save or make notes on, if the technology allows, or to simply make notes about it, if not.

Since the clinical sites will rely on patients and caregivers for administration and data collection throughout the trial, their ability to clearly convey the elements of the study protocol to this group greatly impacts the trial's potential for success. Trials with reduced clinic visits will rely on educational materials delivered to participants electronically. Sponsors should consider including materials in the investigator training that they can then share with the participants.

Is there a potential for a patient's response to a treatment to be confused with another side effect or symptom? Could the wrong data be collected from a device if the settings are wrong? If there are mission-critical pieces of information that must be provided to the participants, sponsors must make sure to call these out during training and, if possible, provide investigators with background on how important they are up front. Consistent sharing of information in this way, from study sponsor to investigator to participant, helps maintain trial consistency. For investigators' convenience, provide a digital toolkit alongside the meeting presentation that they can share with patients and caregivers later.

As with any meeting, investigator or otherwise, knowledge retention is increased by engaging participants. There are many tools to make sure the audience stays alert and engaged with the speakers and the content, including gamification, polling, and even the ability to just ask questions when they arise rather than waiting until the end. More than just “stay awake” tools, these can be effective at gathering information that can be used both in real time and in post-meeting assessment, as well as providing the trial sponsor with the ability to conduct dynamic follow up based on individual site needs.

Polling conducted at the beginning of the training, for example, can gather demographic data about the investigators taking part so presenters know whether they are working with a fairly novice crowd, a group of experienced researchers, or a mix. Polling at the end can determine how well the attendees learned the most important information—and do so before anyone leaves the room. If the results show a significant portion of the investigators are missing a key detail, presenters can redirect their focus to that topic before convening. By keeping investigators engaged, sponsors can gain motivated study sites, provide the necessary training, and uncover any gaps that need to be addressed for a lower risk, efficient clinical trial.

The greatest advantage of polling, however, isn't simple engagement; the game-changer comes from crafting more significant polling questions. For investigator meetings, case-based scenarios that are relevant to the study provide more value to investigators than simple “do you know...” questions. For example, create a case with statistics around a patient. Then ask, “Would this patient be relevant to your study?” By doing so, sponsors can provide real-world perspectives on what types of patients to enroll and which wouldn't be a fit. Make case-based questions complex and as realistic to the study as possible so decisions must be carefully considered before answering. In a DCT, investigators likely won't have the experienced clinical staff of the onsite study center to rely on, so homing in on real scenarios that may occur can speed up their ability to make decisions during the study.

As important as it is to keep the investigators engaged, it's also critical to gather actionable insights that will help make the meetings consistent—and better—over time. Since investigators are coming into the DCT at different times, sponsors will have the opportunity to present many investigator meetings. Through engagement and analytics tools, they should be gathering

information as to not only who attended (the demographics mentioned earlier), but what types of questions were asked most frequently and about which pieces of content; what polling questions were answered incorrectly by the greatest percentage of participants; and what insights or suggestions might have been received through open-ended comments that would help make the next investigator meeting more impactful.

## **Partnering Up Wisely**

When choosing a technology partner, sponsors should look beyond the moments they'll actively be presenting and engaging with investigators during the meeting. Instead, look for a partner who can both engage in the moment and gather the insights needed for looking at a single meeting or a series of meetings related to the same study in order to make strategic changes. Sponsors should also ask for detailed post-meeting reporting that will guide them to specific people or sites who may need additional training to be successful. The technology and expertise to do this exists, so take advantage of it to provide better training that predicts and overcomes some of the challenges investigators might encounter in a DCT.

Most importantly, because decentralized trials are just that, study sponsors need to make sure there is significant and clear communication with the investigators and their sites, and that they do what they can to facilitate clear and accurate communication between sites and the participants. A well-planned and highly engaging investigator training is a critical first step.



**Marc Crawford, MBA**, is CEO of [Array](#), a private company based in Denver, Colo., and focused on providing content engagement technology and services designed specifically for virtual, in-person, and hybrid life sciences events.

## **Not Just Numbers: Big Data, Artificial Intelligence, Real People**

Edited by Gary W. Cramer ([gcramer@acrpn.net](mailto:gcramer@acrpn.net)), Managing Editor for ACRP



If you've been paying attention, you can likely tell from the themes of many previous installments of this news roundup column that I am a fan of science fiction in all its forms. However, I have to admit that I do not have an especially scientifically oriented mindset. That is to say, in my school days I struggled in settings like chemistry and meteorology classes, I quickly forgot everything I ever learned about advanced math once the tests were over, and I eschewed computer programming to instead

take a course in symbolic logic to fulfill the last part of Penn State's expectations for my quantification credits (and loved it!).

All of this is prelude to my amazement that this issue of *Clinical Researcher* has somehow come together with a heavy theme of how not to lose track of how real people fit into where the clinical research enterprise is headed with its current deep dive into big data, artificial intelligence, and all the attendant niceties of machine learning, natural language processing, and a whole bunch of other things I don't really understand. Did I plan it this way? Most certainly not. Am I happy that it happened, anyway? You bet! With so many authors offering me so much material on such topics at the same time, even a Luddite such as myself has to recognize that these things are in the aether, or part of the zeitgeist, or fall under whatever "of the moment" term you wish to use, and I'd be foolish to ignore them. Like I ignore all signs that it's time to get a new smartphone until the one I'm using experiences catastrophic failure and forces the issue.



Anyway, here are excerpts from various announcements (no endorsements implied) that bolster my feeling that, just like the Continuous Quality Improvements and Just-in-Time Managements of years gone by, I will be unable to avoid editing stuff about these new-fangled tech trends for at least the next decade, so I may as well make my peace with them now.

### **Some Tech Trends to Keep Track of for the Sake of Research and Development**

Scientists in biotech, life sciences, and pharmaceutical research are frequently engaged in a race against time when it comes to surfacing new discoveries and bringing them to market, but their momentum is often hindered by antiquated processes around the collection, documentation, and sharing of data. Information provided by [Code Ocean](#) points out that too much of scientists' and data scientists' time is spent on low-level data extraction, cleansing, and manipulation tasks. To address this issue, leading innovators in the biotech industry are pursuing a multi-tiered strategy that includes the following activities, among others:

*Integrating cloud-based solutions.* Cloud solutions offer a smoother, more integrated way to work and minimize collaboration issues between the lab and various stakeholders by providing one place for the data, methods, and software to be shared. According to research from [TetraScience](#), companies are seven times more likely to have to repeat experiments due to data issues that arise when organizations don't keep their scientific data in the cloud.

*Creating standards in analysis workflows.* Data operations, data science, and domain science should all use the same data objects, as well as common methods/analyses like gold standards, which are accessible and easy to manage. Establishing analysis workflow standards for all teams enables the data lineage to be traced forward and backward, and allows for the standardization of analysis workflows across the organization.

*Enabling self-serve.* Up to this point, there has been no such thing as self-serve within models of how research scientists can get at the data collected on their studies while maintaining company-mandated access controls and permission policies. Enabling scientists to have an appropriate level of access to the data, as well as their history, will facilitate better collaboration between study teams and, in the process, immediately accelerate and improve the quality of the results. It will also create more visibility for the work of these scientists within the wider organization.

## **Transforming Clinical Trial Endpoint Analysis with Artificial Intelligence**

Healthcare research technology company Clario has revealed the significant progress it has made in the integration of artificial intelligence (AI) and machine learning into clinical trial data collection through the company's own development and strategic partnerships. More than 30 solutions have been applied, with more than half of them already active on various Clario platforms. The company says that these integrations have led to an evolution in the way it conducts clinical trial endpoint analyses. "By combining AI tools with deep scientific expertise, [we're] achieving faster and more accurate results than ever before," the company noted in [a press release](#) in May. "Furthermore, this integration has enhanced operational efficiencies and patient privacy protection."

"When it comes to AI technology and clinical trials, it's not about one single solution," said Todd Rudo, Chief Medical Officer, Clario. "Clinical trials are complicated and unique to the medicine they are researching, so they require bespoke solutions. ... We currently have [more than] 70 clinical trials enrolled in our various AI models, and our clients and their patients are already realizing the benefits: enhancements in our ability to collect a wide range of digital data types and subsequently analyze them faster and more accurately."

"AI is transforming clinical trials, but we have to be thoughtful in how we develop it for such a complex area," added Achim Schülke, EVP Chief Innovation Officer, Clario. "[Our] approach is to work with our scientific experts to identify meaningful applications of [AI] to improve our performance in data collection and analysis without compromising safety or quality assessments. AI is not a replacement for our scientists, but an effective tool to assist them in their routine work."

## **Partnership Leads to Acquisition with Focus on Tackling the "Data Dilemma"**

Following an almost two-year partnership between the companies, Digital Science, a technology company serving stakeholders in the research ecosystem, [has fully acquired](#) OntoChem GmbH, a company highly specialized in AI-based solutions for finding and extracting key information from internal and external data and text, especially published research. OntoChem will continue

to work as part of Digital Science’s portfolio product Dimensions, a linked research database and data infrastructure provider.

Lutz Weber, CEO of OntoChem, said: “More and more, pharmaceutical companies are rapidly advancing their research with the use of AI, machine learning, and other technologies to accelerate their discoveries and to translate those discoveries into real outcomes. One of the biggest issues for pharmaceutical companies is the ‘data dilemma’—there is so much information to sift through that it can be hard to know where to look or how to focus. Even in one field, such as cancer or diabetes, there is a sea of new knowledge being generated each day in very specific areas of research. This is where our work can help to provide that focus, assisting companies with their discovery and decision-making.”

### **Tech-Driven Solutions to Advance the Patient Experience in Clinical Trials**

Veeva Systems and UCB in May [announced](#) a collaboration that will focus on technology-driven solutions aimed at improving the patient experience and trial efficiency. The collaboration will see UCB adopt Veeva products for electronic patient-reported outcomes and informed consent to provide a patient-centric, digital experience to study participants and actively influence the strategic direction of these and other applications based on learnings. Together, Veeva and UCB say they aim to set a new industry standard for digital clinical trials with multiple applications that meet the unique needs of patients.

### **In Other News...**

Assentia, Inc., a provider of clinical research services headquartered in Raleigh, N.C., in April [announced](#) that it has expanded its global presence by opening an office in Mumbai, India. The formation of this subsidiary and office enables Assentia to establish a hub in the expanding Asia-Pacific clinical trial market, providing support to staff members focusing on global Clinical Trial Agreement negotiation and site payment services in more than 12 countries in the region.





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