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# Clinical Researcher

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

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**Your Tickets for Trial Success**

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## Clinical Researcher

### Association of Clinical Research Professionals

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CHAIR'S MESSAGE

**Revolutionizing Clinical Research: The Profound Impact of AI**

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



In the ever-evolving landscape of clinical research, technological advancements are reshaping the way studies are conducted, data are analyzed, and breakthroughs are achieved. Among the most transformative innovations in recent years, artificial intelligence (AI) stands out as a game-changer. With its ability to process vast amounts of data and make complex predictions, AI is revolutionizing the clinical research industry in ways that were once unimaginable.

**The Power of AI in Data Analysis**

One of the most significant contributions of AI to clinical research is its prowess in data analysis. Traditional methods of sifting through electronic health records (EHRs) and other datasets are time-consuming and often lead to information overload and missed information. AI algorithms excel at identifying patterns, anomalies, and correlations within these datasets, streamlining the research process.

AI also helps researchers in their quest for:

- **Faster Insights**—AI can analyze thousands of patient records, medical images, and genetic data in mere seconds. This speed enables researchers to make quicker decisions, potentially accelerating the development of life-saving treatments.

- Personalized Medicine—AI-driven algorithms can tailor treatment plans to individual patients based on their genetic makeup and medical history. This personalized approach promises more effective treatments and fewer adverse effects.

### **Enhancing Patient Recruitment and Retention**

Patient recruitment and retention have long been bottlenecks in clinical research. AI offers solutions to these challenges by:

- Identifying Eligible Participants—AI algorithms can swiftly identify eligible participants by analyzing EHRs, social media activity, and other relevant data sources. This targeted approach reduces recruitment time and costs.
- Predicting Dropout Rates—AI can predict which patients are more likely to drop out of a trial, allowing researchers to implement interventions to retain them. This improves the quality of data and trial outcomes.

### **Drug Discovery and Development**

AI is also reshaping the drug discovery and development process in exciting ways:

- Drug Repurposing—AI can identify existing drugs with potential new applications. This saves time and resources by reducing time spent in the drug development pipeline.
- Virtual Screening—AI-powered virtual screening of compounds accelerates the identification of potential drug candidates, significantly reducing the time it takes to bring a drug to market.

### **Enhanced Imaging Analysis**

In clinical trials, medical imaging is crucial for assessing treatment efficacy and patient progress. AI is transforming this aspect of research through:

- Automated Image Analysis—AI algorithms can detect subtle changes in medical images that might go unnoticed by a human observer, thus improving the accuracy of diagnoses and treatment monitoring.

- Early Disease Detection—AI can aid in early disease detection by analyzing imaging data for markers that signal the onset of conditions like cancer or neurodegenerative diseases.

## **Challenges and Ethical Considerations**

While AI brings remarkable benefits to clinical research, it is not without challenges, including:

- Data Privacy—Ensuring the privacy and security of patient data is paramount. AI algorithms must be designed to comply with strict data protection regulations.
- Algorithm Bias—AI algorithms hold the biases present in the data they are trained on. Researchers must carefully assess and address potential bias to ensure fair and equitable outcomes.

## **On the Horizon**

In conclusion, the impact of AI on clinical research is profound and far-reaching. From expediting data analysis to enabling personalized medicine and enhancing patient recruitment, AI is revolutionizing the way we approach healthcare research. However, it's essential to navigate the ethical and regulatory challenges associated with this technology to maximize its potential for the betterment of healthcare worldwide.

As AI continues to evolve and help us to reach horizons of medical research once thought of as science fiction, it's clear it will remain at the forefront of our enterprise, driving innovation and ushering in a new era of discovery and improved patient outcomes. Embracing this technological revolution is not just an option; it's a necessity for the future of medicine.



PEER REVIEWED

## **Mapping the Pathway to Take Control of Your Clinical Research Career**

Jessica Fritter, MACPR, ACRP-CP;Carolynn Jones, DNP, MSPH, RN, CRN-BC, FAAN



Did you fall into the clinical research profession? This is a question we have often asked attendees at national clinical research conferences like those held annually by ACRP. Responses have mostly been a resounding “Yes”! Unfortunately, many people find out about clinical research and clinical research careers by accident or in a very roundabout manner, not even realizing that this field was an option prior to suddenly being part of it and maybe or maybe not seeing a clear path forward to making it a career.

Unfortunately for some, an understanding of the multitude of pathways one can take throughout their clinical research career may be lacking at first. { 1 } Moreover, students, mentees, and connections from LinkedIn may be aware of the field but find themselves stymied trying to enter it. They often ask us “How can I get my foot in the door?”

Although pathways into the profession may appear unclear due to a lack of consistency across the pertinent roles and institutions, clinical research careers are predicted to grow at a rate of 9% per year and national efforts have paved the way for transformational improvements. { 1–3 }

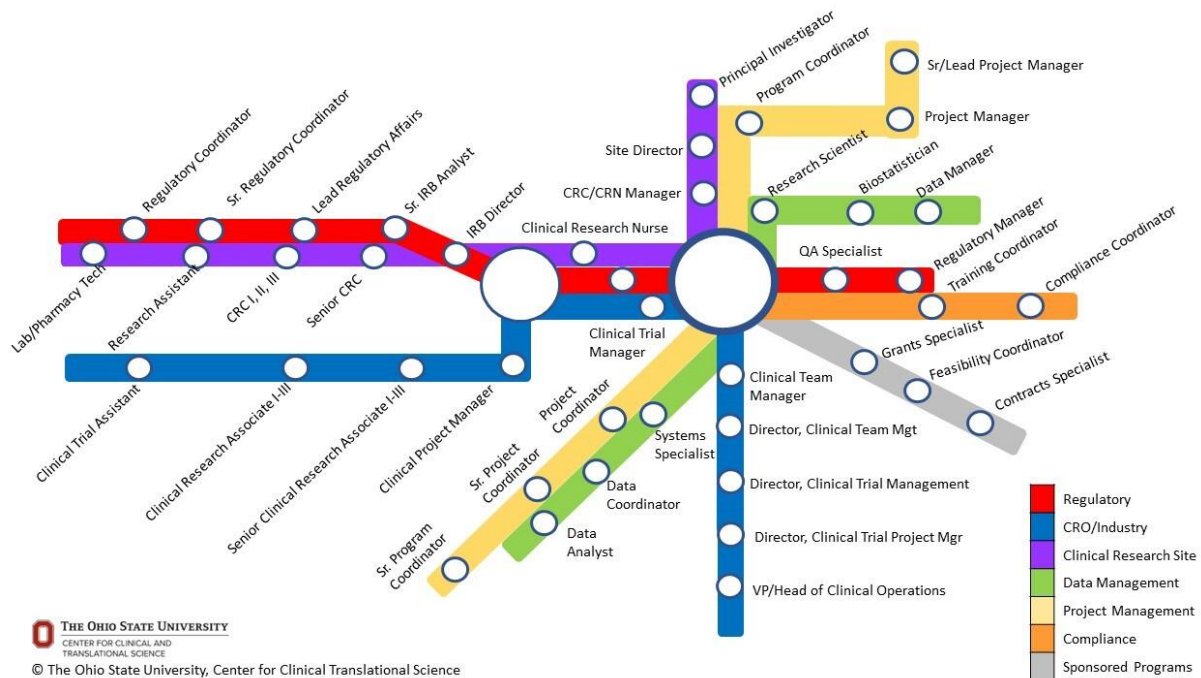


We aim to raise awareness by illustrating varied career pathways in clinical research; to “get the word out” for those who are exploring first-level careers (e.g., your first role pursuing a serious career), for anyone looking at second-level careers (e.g., have had a prior career, but desire a new type of career), and for seasoned clinical research professionals who are exploring new opportunities.

## Mapping it Out

After attending a clinical research conference, we were inspired by a subway (metro) map. If you have ever traveled by metro, you know that you may only have limited options when you first get on at a nearby station, but you can eventually choose from among many different routes offered at various intersecting hub stations. For instance, you can start out on the red line and then, at a subsequent station that offers them, take the blue line or green line, etc. Based on this idea, our map (see Figure 1) illustrates the myriad clinical research career possibilities out there.

**Figure 1: Illustrated Clinical Research Career Map**





Keep in mind job titles may vary across the clinical research industry (with employers including pharmaceutical sponsors, device companies, contract research organizations [CROs], technology and service vendors, regulatory authorities, site networks, academic institutions, and more), which makes having an all-inclusive pathway map difficult to accurately display.

Roles in such areas as study coordination, patient recruitment, pharmacy/drug safety, feasibility, medical writing, finance/billing/contracting operations, statistics, data management, safety reporting, informatics, project management, quality improvement, compliance, monitoring, institutional review boards, laboratory services, and sponsored program administration may appear on organizational charts under a dizzying array of titles. Further, careers not illustrated here include those in the supply chain sector, which is a growing and important career area in clinical research, as well as education.

It is also important to recognize that other new career pathways are evolving as the research enterprise meets the new digital age. However, we aim to raise awareness that there are many careers and pathways to success in the clinical research enterprise by illustrating career titles, junctures, and opportunities to change course.

We wanted to illustrate that there are career pathways based on roles or employers, and that there are also opportunities for switching pathways (e.g., from the red line to the blue line) to reach your ultimate destination. While the exact job title may vary between organizations and institutions, this map can provide insights into the variety of roles one can start and grow beyond in your clinical research professional career.

### **Voices from the Field**

The personas below (see Sidebar) are derived from true stories from professionals we know. Such personas can further illustrate clinical research professional career journeys and spark the imagination.

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## **Sidebar: Three Clinical Research Professional Personas**

### **Jane, RN, CCRC, Clinical Research Nurse Coordinator I**

Jane is a registered nurse who worked for two years in an emergency department in a community hospital before being recruited to coordinate studies there by a doctor who is also a principal investigator (PI) for several clinical trials on potential new treatments for pain.

*“I started working in clinical research one year ago, starting as a Clinical Research Nurse Coordinator I. In my current role, I am responsible for recruiting and consenting participants for six studies. My aim is to progress to Clinical Research Nurse Coordinator II, conducting study visits, collecting data for each study visit, and helping with creating patient educational materials for our studies. Ultimately, I would like to be a clinical research nurse manager, leading a team of study coordinators, negotiating new study contracts, and assisting with new protocol development with my PIs.”*

### **Bradley, BS, CCRA, Clinical Research Associate II**

Bradley started his clinical research career at an academic medical center working as a clinical research coordinator for five years in a cancer center. He then switched career paths and started working for a CRO as a clinical research associate.

*“I would not be where I am in my career if I had not started out in the academic medical center setting. It allowed me to see a trial be run from start to finish from the site perspective. This has greatly influenced my career at a CRO, where I am responsible for monitoring clinical trials across multiple sites and across various clinical departments. This gives me empathy for the roadblocks sites may face and an understanding of how they may cause delays throughout the study.”*

### **Natalie, BS, MS, ACRP-CP, Director of Clinical Research**

Natalie always loved science and medicine but knew she did not want to be an MD or RN. After her undergraduate studies majoring in Biology, she received her master’s degree in clinical research and obtained her certification as an ACRP-CP. She has 10 years of experience and started as a study coordinator, then progressed to a project manager position, and now is a director of clinical research at a private practice research site.

*“I absolutely love what I do and each one of my previous positions has allowed me to navigate where I wanted my career to go. Obtaining my master’s in clinical research and my certification expanded my knowledge of clinical research and gave me confidence when applying to be a project manager. Going from a coordinator to a project manager allowed me to take the skills I knew from being on the front lines to what I needed to know when managing multisite studies. In project management, I was introduced to budgets and contracts, which has been a true asset in my role as Director of Clinical Research.”*

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## **What Skills Do Clinical Research Professionals Need to Acquire?**

Clinical research professionals aim to acquire basic competencies in clinical research based on the [Joint Task Force Clinical Trial Competency Framework](#), which divides skillsets into eight distinct domains: Scientific Concepts and Research Design, Ethical and Participant Safety Considerations, Investigational Products Development and Regulation, Clinical Study Operations (Good Clinical Practice), Study and Site Management, Data Management and Informatics, Leadership and Professionalism, and Communications and Teamwork.{4,5} These competencies are also informed by current federal regulations and International Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines. Other ICH guidelines also inform distinct competencies across roles.

Depending on the role you work in, your skillsets may focus primarily on entry-level skills in some domains, or higher-level skills in other domains. This framework is the standard basis of onboarding training, continuing education training, clinical research certification, and academic coursework. If you want to gain additional knowledge on these skillsets, you can pursue specialized training at your workplace, from professional organizations like the Association of Clinical Research Professionals (ACRP), and through relevant training opportunities, academic courses, books, and articles from a variety of sources.{6}

## **Knowing Your Strengths**

Take a moment for reflection as you embark on this journey. What is your “why”? What is your passion and how does this combine with your skills? A career path is an individual choice and perspective. It is great to set long-term goals, but first, take the time to look introspectively and reflect.

One helpful tool professionals use assesses your innate personal strengths. The Gallup organization provides resources such as *Strengthfinders* that can be a tool for identifying your strengths. {7} Some organizations try to align job roles to an employee's strengths. Not everyone is great at managing, training, or the detailed work of computer data entry. Some may be excellent at patient-facing activities and are clinically oriented. Others are excellent at seeing the big picture and are great project managers. Some individuals may be more introverted or extroverted, thus certain job roles may be more appealing, based on personality traits in addition to innate strengths. There is no one size fits all!

### **Facilitators to Career Entry**

This is a great time to enter the field of clinical research, mainly because of the vast number of job openings in the field across varying employer types. Facilitators to moving into or upwards in clinical research careers include:

*Research the field*—Explore and understand what sorts of roles are available at your target organization. Gain understanding of the key clinical research features of the organization. Do a little research on the company/institution's website.

*Create a good resume*—Avoid trendy resume templates; however, highlighting your skillsets that show your abilities to *organize, manage, create, supervise, or coordinate*. Any team-related skills are important. Check your spelling and use consistent formatting in your resume, preferably listing your accomplishments in each category in reverse chronological order. Keep a running list of all studies you have worked on as an addendum.

*Create a LinkedIn account*—Highlight your skills and begin networking with folks in clinical research areas. Note your account on your resume. A lot of learning and networking happen here!

*Gain formal and continuing education*—One hallmark of a profession is education in the field. There are academic courses and certificates available at the associates, undergraduate, and graduate levels. There are also master's degrees in clinical research,

most of which are 100% online. Depending on what you want to do within your clinical research career, terminal degrees are also available. The [Consortium of Academic Programs in Clinical Research](#) features member institutions that offer clinical research degrees, which could be a resource for students seeking additional information on academic degrees.<sup>{8}</sup> Certification and other licensures require continuing education. Most professionals seek continuing education to stay up-to-date and to progress in their careers. Clinical research is ever changing, and continuing education is essential.

*Join a professional association*—ACRP offers multiple member benefits, including job listings, continuing education, opportunities for involvement, certification, and networking. Professional organizations like ACRP partner with their members to help advocate for, strengthen, and professionalize the field. Also, explore local chapters of your professional organizations and expand your network in your region.

*Become certified*—ACRP offers opportunities for multiple certification examinations. Most certifications require two years of experience working in the field of clinical research before being eligible; however, depending on academic education, there could be variations on this requirement. Certification is a major asset for career progression.

*Know your strengths*—Many career organizations help potential employees explore their personality traits and innate strengths. Do some internal exploration.

*Seek an internship*—Competitive internship programs are emerging in pharmaceutical companies, CROs, and research sites. Many individuals have found a job through internships.

*Explore job openings and job descriptions*—Use search engines like Indeed and Zip Recruiter to explore research positions in your area. More and more positions feature remote (at home) options. Also search directly in company or institution websites to explore openings. And when you get that interview, do your homework by researching the company more deeply.

*Gain experience*—One place that many individuals get their start is at an academic medical center. Working at an academic medical center can position you with access to training and mentoring resources, including exposure to key opinion leaders who are leading the way in researching new discoveries. Often these leaders are funded by the National Institutes of Health or partner with industry to bring new discoveries to human trials. Career paths in the academic medical center setting can be invigorating and rewarding.

## **Conclusion**

Careers abound within the clinical research field. You can assess your skills and strengths, know your why and set a path. Recognize the value of experience, so don't be too quick to jump around once you enter the field. Most importantly, network, network, and network through professional social media (e.g., LinkedIn, ResearchGate), professional associations, and conferences. The job market is strong, and the enterprise is making headway in advocating for clinical research professionals across the spectrum of roles and employers.

Our goal is that one day, students in high school and college will intentionally target clinical research as a professional pathway. We hope that when we ask you at conferences if you “fell” into clinical research, less hands will go up! We hope this article and map will help others see all the opportunities within clinical research and know they can make themselves a rewarding and fulfilling home within this profession.

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PEER REVIEWED

## From the Outside In: An Overview of Four Decades of Progress on HIV/AIDS

Kurt Wolfe, MCR, CCRC



New clinical treatments for diseases are conceived in a laboratory, then tested on animals or through simulations, and finally studied on human beings if deemed promising enough. Moving from point to point in this cycle is rarely a straight line, and costly and time-consuming trial-and-error efforts may be the key strategy for pushing a treatment forward.

This methodology is still the case for the majority of clinical research in today’s environment and, traditionally, studies have been designed without direct input from patient populations. This is becoming less common as researchers recognize that excluding patients from the process of creating effective treatments can lead to misinformation regarding new treatments, risks to generalizability, stigma toward those who are sick, and, overall, less effective treatments.<sup>{1}</sup> The U.S. Food and Drug Administration (FDA) currently mandates the inclusion of patient voices in study development; however, much earlier during the HIV/AIDS crisis, patient advocacy groups had an effective impact on new drug development and disease burden.<sup>{2}</sup>

The HIV/AIDS crisis in the United States and throughout the world devastated the gay and queer community and changed the world’s perspective on how clinical research is performed. A historical review of those who experienced the crisis from the beginning and what changes resulted from those events can provide valuable information for how the field of clinical research may continue to evolve. This four-decade retrospective will tell the story of how the HIV/AIDS crisis changed the process of how clinical research can be performed and, most importantly, how patients and patient advocates were able to make those changes to the system “from the outside in.”

## Background

During the 1970s and early 1980s, the world of clinical research was adjusting from a recent period of major change following World War II. New regulatory efforts such as the Declaration of Helsinki and the Belmont Report shifted the focus of clinical studies onto prioritizing the safety and well-being of research participants. Placebo-controlled, double-blind, randomized clinical trials were determined to be the gold standard for evaluating the legitimacy of any new medical treatment; however, there were still those critics who questioned the ethics and practicality of denying some study participants a potentially beneficial treatment via placebo.<sup>{3,4}</sup> These questions, which were typically only debated by physicians and bioethical philosophers, would soon be topics of great concern to the general population.

Even prior to the beginning of the AIDS epidemic in 1981, gay and queer civil rights advocates also joined in with this sentiment of scrutinizing previously established clinical processes. Advocates had spent the better part of the 1950s and 1960s petitioning the medical community to continue research into health concerns related to gay and queer individuals, as well as delisting homosexuality as a “Sociopathic Mental Disturbance” in the Diagnostic and Statistical Manual of Mental Disorders.

The Mattachine Society of Washington D.C. was one such advocacy group that openly organized small demonstrations to challenge the federal government’s employment restrictions for homosexuals, which was a decision based in part on homosexuality being medically considered an illness.<sup>{5}</sup> This categorization would be removed in 1973 after years of research proved that there was not a significant medical difference between the heterosexual and homosexual populations.<sup>{6}</sup>

Despite these victories, homosexual men (and LGBTQ+ people in general) were still seen as deviant and even dangerous to many in the American public eye, which would lead them to be particularly vulnerable not only to physical harm from AIDS, but to social and political harm as well.

## Part 1: The 1980s AIDS Epidemic

The epidemic moved quickly in June of 1981, as reports to the Centers for Disease Control (CDC) of various opportunistic infections among homosexual men began to increase throughout the United States. Conditions that were often linked to weakened immune systems, such as Kaposi's sarcoma and *Pneumocystis carinii* pneumonia were suddenly being seen in an alarming number of previously healthy patients.{4} About a month after the initial reports to the CDC, news organizations began reporting this new "gay cancer." {7} After hundreds of reported cases within this first year, the name of the condition would change to Gay-Related Immune Deficiency before the CDC eventually settled on Acquired Immune Deficiency Syndrome (AIDS) at the end of 1982.{8}

This decade was one of extreme fear in the U.S., as there were many questions associated with AIDS, such as what caused the condition and how was it spread. This anxiety pushed for a sharp increase in AIDS-related research advocacy from both the medical community and through community grassroots efforts.{9}

One grassroots example took place in 1983 with the publication of a booklet titled *How to Have Sex in an Epidemic: One Approach* by Richard Berkowitz and Michael Callen. This manual was independently printed and distributed in New York City by Berkowitz and Callen, under the medical advice of Dr. Joseph Sonnabend, as a way to help dispel misconceptions regarding the transmission of AIDS within the queer community. While at the time of publication there was no official medical consensus on the mechanisms of how AIDS was contracted, what was clear to the authors was that the known risk factors associated with AIDS transmission needed to be categorized in a digestible and comprehensive format.

At this stage of the epidemic, neither the medical community nor the federal government had been able to engage in such a clear method of scientific communication with the affected population.{10} Ground-level engagement like this would become the bedrock for federal AIDS prevention initiatives within the next several years, and these programs would help kick-start a community-based approach not just to local public health, but global health as well.{11}

By the mid-1980s, the Human Immunodeficiency Virus (HIV) had been discovered as the culprit that caused an infected individual's immune system to decline to AIDS.{12} Clinical trials looking to find a treatment for HIV/AIDS began around this time, and among the first notable agents explored was an unsuccessful anticancer drug called zidovudine (AZT). AZT is part of a drug class known as antiretroviral therapy (ART) that prevents HIV from replicating within the infected patient. With ART keeping the virus from overwhelming the body, the immune system is able to recover and remain healthier for longer, reducing the chance that the patient will develop full-blown AIDS. Although AZT was associated with bone marrow toxicity, headaches, nausea, and insomnia, early results were promising at reducing the progression of the disease.{4,13,14}

At this point in the epidemic, there had not been any sort of recognized treatment for AIDS, so when word of the potential aid AZT could provide arrived, the desperate public put an enormous amount of pressure on pharmaceutical governing bodies to get it into the hands of as many patients as possible. The FDA's regulations over Investigational New Drug (IND) applications made getting this potentially valuable new drug into pharmacies extremely difficult, as unapproved drugs can only be administered on a case-by-case basis after all other treatments have been exhausted. These restrictions prevented the patients who were dying of AIDS from grasping their one lifeline, and this sparked a movement from AIDS advocacy groups to turn their resources toward the FDA.

Efforts made by advocacy groups such as the AIDS Coalition to Unleash Power (ACT-UP) were a major force behind shining a public light on the clinical research process and how more patient-focused rules for how INDs are approved could save the lives of desperate patients. Public outcry and protests brought the concerns of these patients straight to the FDA's doorstep and, through their knowledge of clinical research processes, advocates helped propose a new pathway to allow unapproved INDs to be received by a broader population. This pathway was known as the "parallel track," which essentially allowed for unapproved, but potentially helpful, medications to skip Phase III testing and be given to patients in an extensive post-market (Phase IV) surveillance phase.

While controversial at first, the AIDS Clinical Trials Group as well as the National Institute of Allergy and Infectious Diseases, Division of AIDS led by Dr. Anthony Fauci, ultimately concurred that unapproved drugs of this kind could be given to those who needed them without sacrificing patient safety or the legitimacy of ongoing trials.{4,15} This represented a major turning point not just in the history of the AIDS epidemic, but in the field of clinical research, as the scientific community was made to reflect on its practices as a result of direct community involvement. Despite the advancements being made not just in research, but in the clinical processes for HIV/AIDS, by the end of the 1980s there were more than 100,000 reported cases of AIDS in the U.S. alone and a pervasive culture of stigma toward the disease.{4,16}

## **Part II: The 1990s**

The HIV/AIDS epidemic had affected vast swaths of American culture—from famous musicians, artists, and performers, to regular people just trying to live their lives.{17–19} Pharmaceutical companies were scrambling to launch as many different INDs as possible to meet the demand for a variety of treatment options. After a slow start, the Reagan administration’s response to the crisis had finally begun to establish programs to provide needed aid to patients.{20}

The 1990s continued to see steady activism centered on the rights and protections of those affected by the epidemic, and the successful adoption of the parallel track process helped bolster additional changes to the clinical research field. The National Institutes of Health (NIH) established the Office of AIDS Research to further the country’s efforts to provide new HIV/AIDS treatments and prevention methods, while activists continuously pressured the government to allocate the appropriate funds needed to quell the ongoing crisis. Their efforts resulted in the amount of federal dollars dedicated to ending the epidemic nearly quadrupling by the end of the decade.{21}

ACT-UP proponents were very active during this time, famously holding a highly publicized demonstration in New York City’s Grand Central Terminal at rush hour holding signs with messages such as “One AIDS death every 8 minutes” and “Money for AIDS, not for war” (in reference to the U.S. prioritizing tax-payer dollars for the Gulf War in Iraq and Operation Desert

Storm). Another notable demonstration was at the home of U.S. Senator Jesse Helms, where activists wrapped his Virginia residence in a 15-foot condom to protest his anti-HIV funding voting record.{22}

Research activists also began to shift their focus to populations still being left out of HIV/AIDS treatment groups. In the previous decade, the most visible and outspoken activist voices were usually white, middle-class, gay men, which left little room for groups of those who were equally affected by the epidemic, such as ethnic minorities, women, and hemophiliacs. The early research also reflected this white, middle-class, gay male majority as they were often seen to be the best fit for clinical trial participation over other groups.

People assigned female at birth with HIV/AIDS in particular had difficulty accessing inclusion into clinical trials, as studies at that time were very unwilling to test on anyone who could possibly become pregnant.{23} ACT-UP helped lead the charge in criticizing government-funded research efforts when it came to the inclusion of women and other underrepresented populations, as well as the International Community for Women Living with HIV (ICW), which focused on prioritizing women's inclusion not just in the U.S., but across the globe.{24,25}

The number of potential treatment options expanded during this decade and these were being tested in the same way AZT was in the late 1980s. Unfortunately, as more patients began taking ARTs, scientists started to observe viral mutations that resulted in antiretroviral resistances.{13,14} This prompted research into combination therapies, as single-agent regimens were not creating enough impact to prevent the virus from replicating.

Researchers found that utilizing combined regimens with AZT and medications such as dideoxycytidine and Lamivudine resulted in more favorable outcomes than AZT alone. Other effective medications that emerged around this time included nevirapine and didanosine.{13,26} Highly active antiretroviral (HAART) medications also became a standard treatment.{26} The number of reported U.S. cases in this decade would peak at around 400,000 before beginning to decline going into the turn of the century.{27}

### **Part III: The 2000s to Today**

As the new millennium began, the Clinton administration issued a strong federal response to the still ongoing HIV/AIDS epidemic as a threat not just to national security, but also to global safety.{28} In 2002, the United Nations established a Global Fund to aid countries that were working to reduce their HIV infection rates. Eight of the world's largest economies released a combined statement regarding the international need for investment in HIV/AIDS funding and resources.{29}

As HIV/AIDS became more widely recognized as a global issue, activists pushed for better access to prevention and treatments for middle to lower income countries that wealthier countries already had. The 21st century saw the networks and alliances created in the previous decades flourish into a robust global health community that utilized patient-centered approaches to treat HIV/AIDS and other infectious agents.{11}

With these treatment advancements, the stigmas associated with being HIV+ had lessened, but were not entirely gone. Many U.S. lawmakers still felt that certain policies should be in place for HIV+ patients in the name of protecting public health. Several U.S. states criminalize not disclosing and infected person's status to sexual partners. Critics have responded that criminalizing HIV+ individuals in this way can have unforeseen negative consequences, as this sort of policy incentivizes people with HIV to forgo testing and remain unaware of their status to prevent being accused of knowingly spreading the infection. Health experts have found laws of this kind are counterproductive to reducing the number of new infections and discourage participation in new clinical trials.{30}

This first decade of the 2000s saw continued advancement in HIV treatments and prevention. While HAARTs were thought to be the best way forward in the previous decade, the patient burden of multi-pill, high-toxicity, high-drug interaction regimens made properly adhering to these treatments extremely challenging. Focus instead shifted to single-dose, one-pill-a-day combination ART that could reduce viral loads and increase medication adherence. The success of combination ART therapies led to the approval of the first once-a-day, single tablet regimen in 2006.{26}



HIV prevention for men who have sex with men also took a giant leap forward with the approval of the first daily, oral, pre-exposure prophylaxis (PrEP) medications, Truvada and Descovy in 2012 and 2016, respectively, along with a monthly injectable called Cabotegravir in 2021. {31}

## Conclusion

Across the world, patients with HIV have access to affordable medications that not only allow them to live long and happy lives, but also prevent the infection from being spread. New incidences of HIV in the U.S. have dropped to around 35,000 cases per year in since the 2010s. {32}

The current HIV treatment philosophy of undetectable equals untransmittable (U=U) focuses on reducing the body's viral load of HIV+ patients to a point where it is virtually undetectable, which significantly reduces the virus's ability to spread through sex. {33} These treatments were only possible through the hard work and dedication of activists who were able to affect huge change in a complicated system that has lasted even to today.

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VOICES FROM THE FIELD

## A Professional's Perspective on Participating in a Clinical Trial

*Lisa Osborne interviews WCG executive Peter DiBiaso about his experiences as a drug development professional participating in clinical trials investigating new therapies for Parkinson's disease.*



### **How did you choose the clinical trials that you participated in?**

Since being diagnosed with early onset Parkinson's disease (EOPD) I became aware of several different opportunities, most of them through conversations with my movement disorder specialist and others through my own research. But for the past three-and-a-half years I've been living in Paris, so I am working with a new investigator and learning how to navigate

the French healthcare system. Although, many of the same challenges remain.

The burden of patient recruitment still falls on the shoulders of investigative sites and study coordinators. But my general sense is that staff are overwhelmed, and if you don't prompt them for opportunities, you might not hear about them, even if you are working with well-informed professionals.

### **What has been your experience with the informed consent (IC) process?**

It can be a bit confusing, and I've been through the IC process before. I was familiar with the risks involved, so that wasn't a concern for me. Although for someone who has never participated in a clinical trial, or isn't familiar with the protocol requirements, it's a

confusing document that creates a bit of anxiety, so many patients simply skim through the IC form.

In addition, people with diagnosed conditions who are going into these medical appointments are often nervous, sad, scared, or angry, so they're not hearing everything that's being said. They need time to review the IC document, assess the risks, possibly talk to their partner, friends, caregivers, or family members, and come back with questions.

I like to refer to it as informed decision making because you are not consenting; you want to be educated and truly understand the study expectations. The emphasis should not be on consenting, but on understanding what the form means. The investigator or study coordinator needs to have time to talk to the potential participant, and make sure that, from an adherence standpoint, they understand what's being asked of them. That continues to be a challenge for the entire industry.

### **Has anything surprised you about participating in a clinical trial?**

It has highlighted the importance of small gestures, such as sending a card to participants and their caregivers thanking them for taking time out of their day for study visits. Those human touches reinforce the fact that the site staff are committed to research, and they appreciate the study participants.

Results reporting is another important area. I've never seen any results from any of the studies that I've participated in and I'm still surprised sponsors don't share those.

### **Are staff concerned that participants might not understand the results?**

No, it's a time constraint. Study summaries are written in layperson's language, so anyone can understand them, but it takes a little time to provide context. Study coordinators are very effective at that. I'd love to see the investigators doing it, but they don't always have the time.

### **What impacts did you see from COVID-19?**

COVID-19 demonstrated to the public a lot of the positive aspects of clinical trials and raised awareness. But as participants, we still share many of the same challenges, such as time for appointments and study retention.

During COVID-19, investigative sites struggled to cope with labor shortages and complex protocols. Sponsors fared better as they invested in new studies during that period, as evidenced by the kind of activities and volume of contracted work that we saw at WCG. But without the investigative sites being able to support new studies, the development timelines were impacted.

At WCG, we examined the “site crunch,” as we called it, and the significant pressure put on investigative sites. Even now, they haven’t quite made it back to pre-COVID activity levels.

### **Are you seeing any positive changes after the pandemic?**

Decentralized trials, telemedicine, and a broader adoption of technology received a lot of attention during COVID-19, which was good. But the sponsor industry is proceeding cautiously and still faces concerns with quality and inspection risks.

### **Has your overall experience of participating in clinical trials been positive?**

Yes, it reminds me how dedicated these research professionals are—particularly the coordinators and nurses who are keeping everything together, and the investigators who have all the responsibilities. It’s a lot of work.

### **What is the most pressing thing that needs to change in the clinical trial industry?**

Improved infrastructure support, perhaps with a common platform for electronic data capture systems. There’s not really a commercial benefit for sponsors to all have their own independent systems and designs. For the naysayers, there is precedent—you only need to look at the success of the Clinical Data Interchange Standards Consortium (CDISC) for how industry now manages regulatory filings.



While there will always be some unique elements of a study that sponsors want to keep proprietary, there are no competitive advantages to most aspects of the process, and it would be a big step forward to be able to reduce some of those burdens.

While global standards and more consistency across technology/research platforms won't cut down on the data that need to be gathered, it would be cheaper, and it would provide greater success.

**What key learning would you like to share with other clinical trial professionals?**

I appreciated the investigator taking the time to explain things to me, telling me exactly what was going on during every second of the procedure. That clinical research professional put me at ease.

**Can you describe some of your recent advocacy work?**

Since diagnosis I have run three marathons with my wife to raise funds for the Michael J. Fox Foundation (MJFF). We also hiked Mount Kilimanjaro, which was a great deal of fun, and an incredible experience.

Beyond that, I've represented MJFF policy advocacy on Capitol Hill, and participated in lobbying efforts for research funding. I've met Michael J. Fox on several occasions, and he's just as nice as everyone knows.

More recently, I've been very active on the committee of the Clinical Staging Initiative, which has been developing criteria to define the levels of progression in Parkinson's disease. We have defined six levels of staging with associated biomedical analyses, symptoms, screening tools, and expected duration to serve as a roadmap and help tailor therapeutic interventions to individuals. For example, at a level of four, you're going to start to see some need for levodopa, so that can be added gradually.

It's been an amazing process working with all the different leading researchers and other Parkinson's disease stakeholders. The resulting scientific paper has just been submitted for publication review in *The Lancet*.

We anticipate that Parkinson’s disease research protocols will soon have inclusion and exclusion criteria relating to the staging. Investigators and research sponsors will be able to say, “We are specifically looking at patients at this level, who have this type of condition, and who are using this type of medication,” which will take us closer to precision medicine.



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**SITES & SPONSORS**

## **How to Be a Trial Sponsor of Choice in a Competitive Market**

Matt Smith



In today's evolving landscape of clinical trials, the competition for trial sites with the right patients and strong retention capabilities is intensifying. Trial sponsors are striving to position themselves as the sponsors of choice by fostering collaborative relationships. This is particularly crucial in conducting research in oncology trials, rare diseases, and other high-demand therapeutic areas.

However, clinical trial sites often feel marginalized and burdened by fragmented processes, sudden protocol changes, and challenges in patient recruitment and retention. Furthermore, while new technologies, including artificial intelligence (AI) tools, are emerging, they tend to prioritize sponsors' needs while neglecting the perspectives of the sites that are responsible for trial execution.

Based on my experience working with both sponsors and sites, it's clear that everyone recognizes the importance of change and is eager to make it happen. For sponsors, there's a critical opportunity to take the lead in three key areas to become a sponsor of choice.

## **Bring Site Representatives to the Table During Trial Design**

In our industry, we prioritize the patient experience but often neglect the crucial site experience. What's intriguing to me about this is that sites are stewards of the patient experience—they oversee patient care, facilitate data collection, and play a pivotal role in the overall success of clinical trials. Ignoring their perspective jeopardizes both patient satisfaction and trial outcomes. Developing protocols without input from those on the ground puts the trial at a disadvantage from the start, further exacerbating an already existing issue with the rising number of protocol amendments. In fact, [research](#) indicates that 57% of protocols had at least one substantial amendment, with 45% of those deemed avoidable.

Bringing site representatives to the table early has several advantages. They can help sponsors and contract research organizations (CROs) identify issues in protocol design—including considerations for specific patient populations—and provide insight into areas that could lead to deviations or problems with patient retention. Essentially, sites can act as the “canary in the coal mine,” helping sponsors detect issues in advance.

To bring sites to the table, sponsors can start by finding at least three sites within target therapeutic areas and investing in activities to foster direct relationships with them. Relationship-building efforts are crucial, regardless of whether CROs are also involved in working on behalf of the sponsors. CROs will often engage their preferred sites on a multitude of trials, so the relationship with sponsors can be less of a factor in this case. However, many sponsors, including large pharmaceutical and biotechnology companies, are already opting to maintain direct relationships with sites during the trial process.

Sponsors can further engage sites in the trial design process by providing them with the draft protocol and addressing any specific questions or concerns in a review call. Sites are experts on trial operations and have valuable insights into what will likely work and what won't; the most seasoned site leaders have likely seen hundreds—if not thousands—of trial protocols come across their desks, so they can provide insights on what makes a good design. Utilize that expertise—they have so much knowledge to offer.

## **Prioritize Site-Centric Technologies**

A significant portion of the technology utilized at sites aims to enhance efficiency, ensure regulatory adherence, and mitigate risks. This encompasses tools such as electronic medical records for patient records, a clinical trial management system for trial scheduling and patient visits, and others. Sites display remarkable resourcefulness, often devising a workflow solution by amalgamating various commercial solutions, spreadsheets, and in-house tech innovations. The absence of these systems can hinder sites from expanding and conducting multiple trials while effectively managing risk and compliance.

A prevalent challenge arises from the fact that technological solutions are frequently developed and chosen primarily with sponsor needs in mind, without consideration to site workflows or experience. This leads to sites grappling with a surplus of tools without streamlined solutions for facilitating their day-to-day operations. On an average basis, sites use around [12 distinct technological](#) components in each trial. Considering many sites oversee multiple simultaneous trials, the burden becomes clearly evident.

To bridge the gap between incongruent processes that aren't optimized for site staff, sponsors can play an active role in selecting technology tailored to site needs when evaluating vendor solutions. Inquiries should focus on the integration and data exchange capabilities of new solutions with existing site tools.

User experience is equally vital; assessing how platforms are perceived by sites and patients and engaging sites for feedback during the review process are crucial considerations. Opting for site-centric technology can bring benefits for all stakeholders—from sites and sponsors to CROs and vendors.

Utilizing site enablement technology, processes and platforms that seamlessly integrate with sites' workflows can bring about substantial advantages for the broader trial ecosystem. Such technology alignment reduces the need for redundant data input, thereby reducing the risk of errors and duplicative effort by site staff. Additionally, it brings about insights from data more quickly by eliminating the need to enter results into multiple systems, often well after patient visits.

## **Establish Universal Processes**

While it is important to recognize the value of platforms spanning the entirety of a trial, there remains room for enhancing the overall workflow. Currently, workflows and systems are often compartmentalized and centered around specific trial aspects or processes. This raises the question of whether we are potentially overlooking opportunities to leverage data and solutions from one phase of the trial to inform and enhance downstream processes.

Although the idea of a handful of all-encompassing solutions overseen by a select few vendors may seem ideal, it's not a practical reality. Such an approach would clash with the diverse and intricate requirements of various trials. Currently, platforms are emerging for establishing vertical connections that link sites, sponsors, CROs, and vendors. However, as the clinical research enterprise moves toward the goal of system interoperability, we're witnessing a shift toward platform solutions that foster horizontal connections. These solutions are adaptable across a broader range of trials and are seamlessly integrated into site workflows.

Sponsors, as the financial backers of trials, wield the necessary influence to implement these changes. By viewing the trial workflow as an interconnected ecosystem rather than isolated components, we can quickly identify areas for improvement that need a champion to lead the charge. The essential components are already there—they simply need to be put together.

## **Become the Sponsor of Choice**

In an increasingly complex and competitive clinical trial landscape, it is crucial that sponsors rethink the role of sites. By involving site representatives early in the trial design process, sponsors can tap into their wealth of experience and insights, ensuring that protocols are not only patient-centric but also operationally feasible.

Prioritizing site-centric technologies is another crucial aspect, as it empowers sites to manage multiple trials efficiently, reducing redundancies and the risk of errors. The synergy between sponsor-selected technology and site workflows paves the way for a smoother, more integrated trial ecosystem. Moreover, by embracing universal processes that foster interconnectedness across all stages of a trial, sponsors can lead the charge in driving comprehensive and impactful change.

As the driving force behind clinical trials, sponsors have the unique opportunity to reshape the industry by aligning incentives, fostering collaboration, and placing sites at the heart of trial innovation. Through these strategic initiatives, sponsors can emerge as innovators in clinical trial execution, setting a new standard of excellence in a competitive and evolving landscape.



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## **Pushing for Better Clinical Trial Design for Rare Diseases**

Haley Quinn



Imagine a world where a rare disease diagnosis no longer spells a journey of uncertainty and pain. Instead, it begins a collaborative journey where patients, healthcare professionals, and researchers unite to uncover personalized solutions. In this world, trial design isn't constrained by rigid parameters; it flourishes in the realm of possibility, embracing the nuances of each patient's experience.

Amid the consistent stream of medical breakthroughs and groundbreaking treatments making waves in the news, it's all too common to inadvertently disregard the plight of millions living with rare diseases. These conditions, frequently concealed in obscurity, present intricate challenges that elude swift diagnosis and effective treatment. New research has highlighted the dire consequences of neglecting these conditions, pointing to the critical need for better trial design and patient engagement.

Consider this staggering statistic: A recent study found a lack of treatment for rare diseases is associated with a 21.2% increase in total costs per patient per year. When extrapolated, the societal cost of neglecting the 7,000 known rare diseases in the U.S. could range between \$7.2 to \$8.6 trillion annually. It's a much-needed wake-up call, underscoring the urgency of clinical research that can help to alleviate the burden of living with rare diseases. { 1 }

Let's explore the convergence of patient experiences, trial design, and collaborative endeavors poised to reshape the healthcare landscape. As we navigate through the intricate layers of this

topic, we will uncover how the consideration of patients' backgrounds, daily symptom management, and a holistic approach to trials can ignite transformative change.

### **The Evolution of Trial Design: Beyond Traditional Parameters**

Traditionally, clinical trial design has adhered to specific parameters that, while structured, may not fully encapsulate the reality of patients' lives. The journey of a rare disease patient is often laden with complexities that extend beyond the boundaries of these parameters. As we shift our perspective, we understand that a more comprehensive trial design can yield richer insights and more effective treatments.

Picture a patient diagnosed with a rare disease who has faced numerous challenges, from misdiagnoses to ineffective treatments. These struggles are rooted in their unique experiences, often overlooked in antiquated clinical trials. By incorporating real-world data, predictive analytics, and technology, we can expand the horizons of trial design. This evolution allows us to consider not only medical factors but also patients' geographic locations, socioeconomic backgrounds, and the overall impact of their condition on their daily lives.

Since rare diseases often exhibit unpredictable symptom fluctuations, tailoring trial schedules to accommodate these fluctuations can reduce patient burden and provide a more accurate assessment of treatment effectiveness. For instance, flexible appointment times or remote monitoring may enhance patient engagement.

### **A Collaborative Approach: Paving the Way for Patient-Centric Care**

The heart of revolutionizing trial design lies in collaboration. Pharmaceutical companies, advocacy groups, healthcare professionals, and patients must unite to drive change. The patient journey, fraught with uncertainties and challenges, becomes the compass guiding these collaborative efforts. The results can be remarkable when patients are empowered to actively participate in shaping their treatment paths.

Envision a clinical trial that not only evaluates the efficacy of a treatment but also considers the financial burden on patients, the emotional toll of their condition, and the accessibility of the

treatment itself. Such trials yield more robust data and foster a sense of inclusivity and understanding.

In the context of rare diseases, patient experiences are often defined by their day-to-day symptom management. Incorporating patient-reported outcomes into trials allows patients to report on their symptoms, providing valuable insights into treatment efficacy beyond traditional clinical metrics. For example, tracking pain levels, fatigue, or mobility can reveal the true impact of a treatment on a patient's quality of life.

When patients are heard and their experiences acknowledged, they are more likely to engage fully in the trial process, leading to more accurate results and, ultimately, more effective treatments.

### **Empowering Patients: A Catalyst for Change**

In the United States, the [prevalence of rare diseases](#) is an often-overlooked reality, with nearly 10% of the population, equivalent to around 30 million individuals, affected by a rare disease. What's even more disheartening is that an estimated 95% of these rare diseases lack a U.S. Food and Drug Administration (FDA)-approved treatment, leaving patients in a state of uncertainty. For the 5% that do have available treatments, the path to access remains riddled with barriers, including exorbitant costs, protracted timelines, and a critical lack of comprehensive support.<sup>{2}</sup>

[My own journey](#) as a rare disease patient underscores the transformative potential of patient empowerment. For 26 years, I grappled with an undiagnosed condition, enduring countless surgeries and dislocations. My experience prompted me to shift my focus toward building communities and support systems for individuals like me. I realized my story was not a singular instance—countless others were navigating similar challenges. This realization eventually led to receiving a diagnosis and has fueled my commitment to optimizing the patient journey within clinical trials.

Through collaborative efforts and a patient-centric approach, I found the specialized care I needed. My journey culminated in achieving seemingly simple goals that held monumental significance for the quality of my life, such as performing daily tasks like walking my dog or

putting on a shirt without the constant fear of dislocations. My experience is a testament to the impact of both novel and personalized care.

### **A Vision for Tomorrow: The Future of Healthcare**

As we envision the future of healthcare, a new definition of success emerges—one that extends beyond clinical outcomes and profitability. Success, in this context, is measured by the positive impact on patients' lives, the reduction of societal healthcare costs, and the empowerment of individuals to navigate their health journeys with dignity and hope.

Patient engagement isn't a mere checkbox—it's a fundamental pillar of healthcare transformation. Patients become active partners, contributing insights that drive the development of treatments tailored to their unique needs. Through open channels of communication, patients and researchers exchange knowledge, share successes and challenges, and co-navigate a journey to improved health.

Technology plays a pivotal role in this transformation. Predictive analytics harness the power of data to anticipate patient needs and optimize trial outcomes. Real-world evidence becomes a treasure trove of insights, painting a better picture of patients' lives beyond the confines of clinical settings. Telehealth and digital platforms ensure patients have continuous access to care and support, breaking down geographical barriers and improving quality of life.

In this future, the healthcare ecosystem thrives on collaboration. Pharmaceutical companies, advocacy groups, policymakers, medical providers, and patients converge to drive change that ripples through the industry. The focus shifts from short-term gains to long-term impact, and from isolated efforts to synchronized movements for change.

Patient-centric trial design isn't a solitary destination—it's a roadmap to a future where healthcare is a collective endeavor, where the stories of patients shape the narrative of progress. Together, we can bridge the gap between treatment and transformation, forging a healthcare landscape that is economically sound, emotionally resonant, and undeniably patient-centric.

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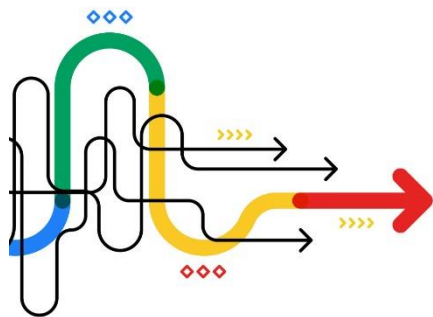


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CULTIVATING QUALITY

## Guidance for Preparing Standard Operating Procedures (SOPs)

Olena Chervonenko, MS



Standard operating procedures (SOPs) play a vital role in ensuring quality, compliance, and safety across a pharmaceutical company’s operations. SOPs are key to ensuring users follow current requirements and best practices and perform tasks consistently and uniformly.

An SOP is a documented set of step-by-step instructions that outline the approved methods and practices for carrying out specific tasks or processes within an organization.

When writing SOPs, it’s important to strike the right balance between providing enough detail and avoiding excessive complexity. Insufficient detail increases the likelihood of users improvising on the spot or following widely used, but perhaps inadequate, methods. On the other hand, excessive information can lead to confusion, errors, and mistakes.

In the pharmaceutical industry, improvising or deviating from established methods can have serious consequences and may result in the company becoming noncompliant with one or more of the internationally agreed-upon “Good x Practices,” where “x” may stand for Clinical,{1} Manufacturing,{2} Laboratory,{3} etc.

SOPs must ensure the robustness, traceability, and integrity of a Pharmaceutical Quality System (PQS) of an organization and contribute to maintaining quality, safety, and compliance standards within the organization.

## **Robustness of the PQS**

SOPs provide a systematic and documented approach to performing critical tasks and processes within an organization. By outlining specific procedures, controls, and requirements, SOPs help ensure the robustness of the PQS. They establish a framework that promotes consistency, traceability, and accountability in all operations.

SOPs incorporate safety considerations and guidelines to mitigate risks and protect personnel, patients, and the environment. They outline business workflows, safety protocols, personal protective equipment requirements, handling procedures for hazardous substances, and emergency response measures. By adhering to SOPs, organizations promote a culture of safety and minimize the potential for accidents or incidents.

In short, SOPs are essential tools in assuring the robustness of the PQS.

## **Traceability**

Ensuring the traceability of the PQS is a critical aspect of SOPs within the pharmaceutical industry. Traceability provides a clear and documented path that demonstrates the implementation and effectiveness of the PQS. Here are some key considerations to incorporate traceability into your SOPs:

*Documented References:* SOPs should reference the relevant sections of the PQS documentation, such as quality manuals, policies, and guidelines. This ensures that SOPs are aligned with the overall quality system and current edition of guides.

*Version Control:* SOPs should have a version control system in place, indicating the specific version number, date of revision, and any relevant updates. This allows for easy identification of the most current version and facilitates traceability.

*Cross-Referencing:* SOPs should cross-reference other related SOPs or documents within the PQS. This ensures that interdependencies between procedures are clearly identified and maintained.

*Change Control Process:* The revision history of an SOP should clearly outline the specific changes that were made, accompanied by a linked change control document. This document should include thorough documentation of any modifications to the SOPs, along with justification and, if applicable, a risk assessment. This facilitates traceability and identification of the chronology of changes.

By incorporating these traceability elements into your SOPs, you establish a clear link between the procedures outlined in the SOPs and the overall PQS, ensuring transparency, compliance, and effective quality management.

### **Data Integrity**

Data integrity is a critical aspect of SOPs within the pharmaceutical industry. It ensures that data generated, recorded, and reported during operations are accurate, complete, and reliable. SOPs must declare data integrity principles to prevent data manipulation, fraud, and errors. Key considerations for maintaining data integrity via SOPs include:

*Data Recording:* SOPs should outline the proper methods for recording data accurately, including clear instructions on data entry, identification, and verification.

*Audit Trails:* SOPs should define procedures for creating and maintaining audit trails, which provide a chronological record of data changes, ensuring data integrity and traceability.

*Data Security:* SOPs should incorporate measures to protect data integrity, such as access controls, data encryption, and regular data backups.

### **Bringing in the Right People**

It is important to involve quality assurance (QA) and senior management in all stages of SOP creation -- from ideation to assessing the effectiveness of implemented SOPs.

The QA department plays a crucial role in ensuring the effectiveness of SOPs within the pharmaceutical industry. QA staff are responsible for overseeing the development, implementation, and maintenance of SOPs to guarantee compliance with industry regulations



and standards. Chiefly, they are responsible for SOP review, collaborating with subject matter experts to ensure SOPs are accurate, comprehensive, and aligned with regulatory requirements.

Senior management plays a key role in supporting and driving the effective implementation of SOPs. Their responsibilities include:

*Policy and Strategy:* Establishing clear policies and strategies that emphasize the importance of SOPs in ensuring quality, safety, and compliance throughout the organization.

*Leadership and Communication:* Promoting a culture of quality and compliance, fostering a shared understanding of the significance of SOPs at all levels of the organization. Senior management also communicates expectations, provides guidance, and encourages employee engagement.

*Continuous Improvement:* Supporting a continuous improvement mindset by encouraging feedback, monitoring of performance metrics, and implementing initiatives to enhance SOP effectiveness.

## **Focus of Inspection**

During inspections, regulatory authorities and auditors focus on evaluating the implementation and effectiveness of SOPs. They assess whether the organization has well-documented and controlled SOPs, that these SOPs are followed, and that they are in compliance with regulatory requirements. Key areas of inspections related to SOPs include:

*Process Description:* Inspectors assess whether the organization has cohesively documented all GxP relevant activities.

*SOP Availability:* Inspectors verify that SOPs are readily available to personnel and accessible in relevant areas where tasks are performed.

*Adherence to SOPs:* Inspectors assess whether employees follow SOPs consistently, ensuring that documented procedures are being executed as specified.

## **Further Considerations**

When creating or updating SOPs, it is important to keep in mind the following points to avoid unnecessary complexity:

*Author and Reviewer:* The author of the procedure should be someone who performs the task or possesses a deep understanding of it. They should strike a balance between providing adequate detail and avoiding excessive elaboration. The reviewer's role is to ensure that the SOP achieves the appropriate level of detail.

*Ask Why:* Simplify and improve the workflow by questioning the necessity of each step in the SOP. This technique involves creating a comprehensive list of all the steps in a work process and critically evaluating their purpose.

*Field Testing:* Red line the procedure in the field to assess its relevance and coherence. This practice involves documenting and accurately recording the process while onsite, often accompanied by clear photos that can be included in the SOP.

*Embrace Simplicity:* Lengthy and intricate SOPs are challenging to follow. Strive to keep SOPs simple and user-friendly while ensuring that all important steps are included. Complex tasks can be broken down into smaller sub-steps. Sentences should generally be kept short to ensure clarity.

*Visual Aids:* Humans process visual information more easily than text. Improve the understandability of SOPs by incorporating photos, drawings, and flowcharts. Visual aids can significantly assist in conveying complex information.

*Minimize Involvement:* Involving fewer individuals in a task reduces the likelihood of human error. Streamlining the number of people involved in a task enhances efficiency and accuracy.

*Audience Consideration:* SOPs should be tailored to the education, experience, knowledge, and abilities of the personnel who will use them.

*Language:* SOPs should be written using vocabulary relevant to the area of use, experience, knowledge, and abilities of the personnel who will use them.

*Testing and Verification:* Before finalizing an SOP, conduct tests with individuals who will use it regularly. Their feedback can help identify unclear information, missing steps, or incorrect sequencing. It can also be beneficial to have someone with limited knowledge of the process test the SOP to ensure its accessibility to a broader audience.

*Preserve Simplification Efforts:* During the review process, carefully evaluate any additional or removed steps. Justification should be provided before incorporating any changes, being cautious to maintain the simplified nature of the SOP. This approach ensures that deviations are properly identified through root cause analysis.

*Regular Review and Revision:* Seek feedback from those who have direct experience using the SOP after several weeks of implementation. Evaluate clarity, effectiveness, readability, and ease of use. Revise the SOP based on the feedback received.

*Keep SOPs Updated:* Regularly review and update SOPs to align with current practices and requirements. Failure to periodically review and update SOPs can quickly render them obsolete. A recommended review frequency is every two to three years. The review frequency should be justified.

## **Conclusion**

By following these guidelines and incorporating the necessary elements, SOPs can effectively guide pharmaceutical industry professionals, promote efficiency, support compliance and data integrity, and contribute to the overall success of an organization.

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## Resources

A list of SOPs required by the U.S. Food and Drug Administration, the European Union Guideline to Good Manufacturing Practice (GMP), and the World Health Organization for GMP activities can be found at <http://www.gmp-compliance.org/gmp-news/which-sops-are-required-by-gmp>.

For Good Documentation Practice (GDP), the Health Products Regulatory Authority in Ireland has published a guidance document that includes the SOPs that are needed for compliance with GDP and details the general framework for each SOP at <https://www.hpra.ie/docs/default-source/publications-forms/guidance-documents/ia-g0038-guide-to-quality-system-for-general-sale-wholesale-distributors-v2.pdf?sfvrsn=14>.

European Medicines Agency Procedures, EMA: <https://www.ema.europa.eu/en/procedures>

Manual of Policies and Procedures, FDA: <https://www.fda.gov/media/90280/download>

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PRESCRIPTIONS FOR BUSINESS

## 5 Keys to the Kingdom for Making Successful Acquisitions in the Clinical Trial Industry

Paul Evans



Mergers and acquisitions are part and parcel of doing business in today's clinical research enterprise, and when you've been involved in more than 20 acquisitions totaling more than 80 clinical trial sites since December 2017, you certainly learn a few things along the way.

You learn how to identify high-performing people and organizations, how to bring out the best in them as they join your organization, and how to improve the patient experience in clinical trials—endeavoring to shorten the timeline for vital drugs and treatments to become available to those who need them the most.

At Velocity, we've been fortunate to build upon our core business and set of processes to expand our therapeutic expertise. We have done this by making site acquisitions across multiple U.S. states and countries, over the past few years.

As you may imagine, it's not always been a smooth ride, navigating the acquisition and fusion of disparate cultures, specialties, and other variables. But it's exactly that hybrid vigor we seek when looking for new organizations and professionals to integrate into our corporate family. Just as the science of clinical trials benefits from patient diversity, so does the workforce and the broader industry.

In addition to my own reflections, I've culled some best practices and insights from team members who shared their perspectives about the best ways to successfully acquire a new entity.

## **It Begins and Ends with People**

I'm going to focus on five key areas, but the human element of any acquisition cannot be underestimated. I'd argue that if you successfully mesh cultures, the other issues can become somewhat secondary. Conversely, I'd suggest that if you fail to mesh cultures effectively, you begin the process at a significant, if not terminal, disadvantage.

With that in mind, here are the five top considerations for acquiring and integrating clinical sites that we would like to share based on lessons learned—sometimes the hard way—before, during, and after the acquisition process. For better or worse, an acquisition is a marriage of sorts and compatibility is vital to its success.

**Cultural Fit:** Assess the cultural fit of the organization and its people. Are they open to new ideas and approaches? As the organization doing the acquiring, we have a clear vision and clear way of doing things operationally, and we adopt a fully integrated network model. While we're open to learning new and better ways to achieve something, we also know our model has worked well and is worth emulating. We aren't looking for franchises where we simply put up our logo over the previous company's name, rather, we are looking for partnerships where acquisition targets buy into our model. Our model is designed to provide sponsors and contract research organizations (CROs) with what they need—streamlined clinical processes, assurances on data quality, and quick start-up times. Our sites are fully integrated via a centralized infrastructure and common technology backbone, including centralized budgets and contracts, business development, standard operating procedures (SOPs), and a robust operational oversight team. This streamlined approach allows for superior patient enrolment and consistent, high-quality data delivery. As a result, CROs and biopharma companies can benefit from simplified access to international clinical research. Potential site acquisitions need to align and buy into this operating model for everyone involved to call the relationship a success.

**Company Reputation:** Find out what *others* think about the site being considered for acquisition. Assess the quality of the site and its reputation in the industry. You can begin to paint this important picture in a number of ways, including reviewing their audit history with the U.S. Food and Drug Administration (FDA), site SOPs, and other work instructions. Gather

anecdotal evidence from sponsors, CROs, or individuals within your company who know of, or have worked with the site. You'd be surprised how much valuable information you can learn from these activities. In some cases, the information can help make for a better transition during the acquisition. In some cases, you may decide the target is not the right match for your organization.

**Site Growth Potential:** In the research industry, sites are valued based upon a multiple applied to the net profitability generated by the site. There is a correlation between the multiple paid and the level of earnings and the industry generally pays more for a site with higher earnings. The multiple paid incorporates future growth assumptions. How is the site going to grow in the future to justify the multiple purchase price? Is the site able to expand therapeutically? These types of questions need to be considered to ensure you are spending your funds wisely.

**Therapeutic Fit:** Do the site's therapeutic capabilities fit into your strategic growth objectives? Is there a willingness to expand therapeutic capabilities or is the site set upon focusing in one area? A site that focuses on a narrow therapeutic area will inevitably suffer the consequences of the ebbs and flows in industry pipeline. We are looking for sites that have the interest in or capability to expand their areas of expertise. For example, we recently closed on exciting acquisitions of the Impact Research Institute in Waco, Texas and the Liver Institute in Seattle, Wash. Adding these sites to our team will allow us to expand our research work in the area of fatty liver disease and metabolic dysfunction-associated steatohepatitis (MASH).

**Access to Patient Population.** Discern the quality of the site's patient database and its access to minority and at-risk patient populations. Does the patient database include minority patients who have either participated or shown interest in a research study? Given the FDA's industry guidance requiring the enrollment of minority study participants, the evaluation of the site's patient catchment area is an important factor to consider. Look to see if the site is located in an area that helps to facilitate the enrollment of minority patients and if the patient database is fully representative of the demographics of the region. Often clinical research sites are in predominantly white and affluent areas, which creates a barrier in the participation of some minority patients. Moving sites closer to diverse communities makes clinical research more accessible for people who are interested in taking part. Removing long travel burdens and

reducing the need for time taken off work to participate in a study could also result in paying smaller stipends for sponsors.

### **Worth the Effort**

There's something uniquely exciting and rewarding about finding new organizations to work and grow with to advance the conduct of clinical trials. It isn't always easy finding the right partners and acquisition targets, but hopefully these ideas will help you and your organization as you consider your own future growth opportunities. I can assure you it is worth the effort.

I believe our acquisition efforts have been successful in large part because we've made such a concerted effort to address, respect, and mesh cultures. In addition, our centralized structure helps streamline some operations for our new partners, while we also empower them to put even more energy into the effective patient care and recruitment efforts that have already served them so well—and made them people we wanted to work with in the first place.

Patients deserve our best. By exploring new ideas and new ways of working together, we can deliver our strongest and most effective results to ensure patient safety and promote an even higher level of care fueled by new, exciting, and innovative drugs, devices, and treatments.



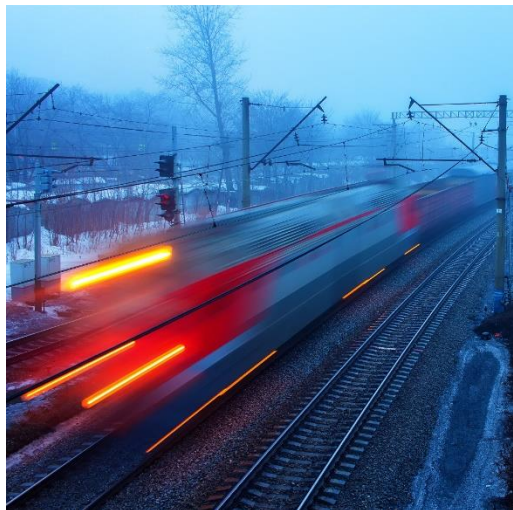
**Paul Evans** is President and CEO at [Velocity Clinical Research](#) and a former Chair of the Association Board of Trustees for ACRP.



GOOD MANAGEMENT PRACTICE

## Ensuring Timely, Secure Delivery of Therapies for Rare Diseases

Dea Belazi, PharmD, MPH



Clinical trial research teams are increasingly focused on the development of specialty drugs and cell and gene therapies (CGTs) to provide an estimated 300 million people worldwide with potentially lifesaving, curative treatment for the 7,000 known rare diseases. Today, there are more than 2,000 clinical trials under way{ 1 } with 200 in Phase III targeting patients with rare, complex diseases who often face death, disability, or poor quality of life from lack of effective treatments.

As specialty drugs continue to be the main category in the U.S. Food and Drug Administration's (FDA's) pipeline for new approvals as of mid-2023 and it has been projected that 13 new cell or gene therapies could be approved in the U.S., Europe, or both by the end of 2023,{ 1 } optimizing the supply chain must a priority throughout the pre-commercialization phase of drug development.

Among the myriad challenges to researchers are the unique requirements of these new, innovative therapies and the burdens tied to establishing protocols for flexible, agile supply chain logistics in support of their research and development. A focus on cold chain design, which begins when the cell-based raw material leaves the cell bank or transplant center and ends with arrival at the transplant center for transfusion, often requires engaging a logistics partner with deep experience in rare diseases early enough in the planning stage. All designs require effective response to the distinct, just-in-time demand requests that account for delivery interruptions, shortages of resources, dosing site storage flexibility, and warehousing capacity.

The need for risk management is paramount, given the multiple stakeholders involved in the supply chain. Contingency plans should be in place to safeguard a zero-error environment. By implementing best practices and leveraging advanced technologies, research teams can help to ensure a supply chain that is robust, efficient, and compliant. The process to identify efficiencies that could speed up therapy for small patient populations is highly relevant to CGTs, in particular, where complex and multifaceted delivery routes necessitate close coordination and collaboration between stakeholders to ensure product integrity and security all the way to the administration site.

In cases of specialty/orphan drugs under development, there is heightened need for temperature controls to maintain stability and drug efficacy for these products, which are largely biologics. A reliable distribution partner with deep experience and expertise with rare disease can provide fully compliant cold chain logistics support for all temperature, shock, vibration, and atmospheric pressure-sensitive orphan drug therapies. This level of support will maintain product availability and efficacy from the manufacturer to the site of care—even in the most challenging climates.

Monitoring temperature and location, as well as unique logistics-related challenges, is increasingly important in these complex formulations where the loss of product can be costly and time-consuming to both the supply chain and the patient.

### **Spotlight on CAR-T Cell Therapies**

There are currently six FDA-approved CAR-T cell therapies available to patients in both the U.S. and Europe to treat various blood cancers.<sup>{2}</sup> The supply chain of cellular therapy is unique and distinct from that of other medical therapies. Cells are harvested from a living donor, typically in a clinical location, and then sent to a processing facility for selection, expansion, and genetic modification before they arrive at a clinical location for administration. Experience shows that the cells must remain viable and functional along this complex supply chain, and that ineffective methods of preservation limit growth in the use of cell therapies. Effective methods of cryopreservation permit coordination of the therapy with patient care and completion of safety and quality control testing.

Many factors in cryopreservation affect the outcome of a cell therapy, including formulation and introduction of a freezing medium, cooling rate, storage conditions, thawing conditions, and post-thaw processing.<sup>{3}</sup> Industry experts report that post-thaw processing of cryopreserved cells varies greatly, with some studies infusing the cells immediately upon thawing, some diluting the cells in a carrier solution of varying formulation before infusion, some washing cells to remove cryoprotective agents, and others reculturing cells to recover any viability or functionality lost due to cryopreservation. To address these variables, many clinical trial researchers depend upon a third-party resource to advise on these decisions and augment in-house expertise.

### **Demand Forecasting and Supply Chain Logistics**

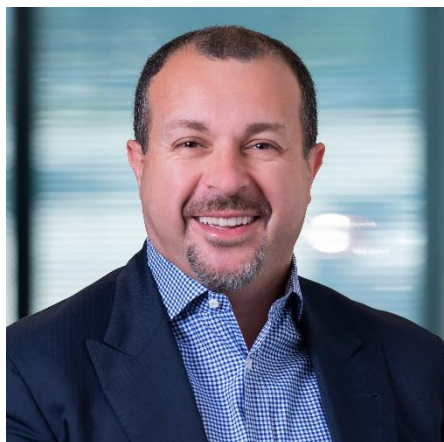
While it is often difficult to accurately predict the manufacturing capacity that will be needed when a new, innovative product is finally launched, the advent of CGTs requires demand forecasting unencumbered by the uncertainties of the CGT supply chain or the absence of long-term historical data. Despite these issues, manufacturing capacity should be matched carefully with demand so that patient-specific doses are delivered just in time to sites of care,<sup>{4}</sup> including independent facilities, hospital-based centers, clinical trial sites, and the home setting. Experts advise that beginning dynamic demand forecasting as early as three years before the actual launch optimizes the supply chain design.<sup>{5}</sup>

Accurate forecasting should establish a digital supply chain thread that includes real-time track-and-trace data on critical information such as the location and quality of cells extracted from patients for autologous cell therapies, reports that follow the patient journey, and market intelligence that captures payer reimbursement levels. Precise forecasting also requires specific data on the size of the eligible patient population, including real-world evidence of treatment outcomes and quality-of-life scores for patients.

All providers in the supply chain should be part of the chain of identity and chain of custody, capable of tracing and recording every step of the product's journey and every person/container involved, from the sourcing of raw materials to final delivery to the patient.

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BY THE NUMBERS

## Facts and Figures at Play in Today's Clinical Research Enterprise

Curated by Gary W. Cramer, Managing Editor for ACRP



**\$500 million** The Biden Administration's investment across 13 projects as the latest installment in the federal government's Project NextGen, a \$5 billion plan to develop new COVID-19 treatments, vaccines, and ways of delivering them. The Health and Human Services Department this summer channeled \$1.4 billion to similar goals.

Source: <https://www.statnews.com/2023/10/13/covid-vaccines-castlevax-codagenix-gritstone/>

**174%** The increase in value of venture capital investments in the pharma/biotech sector from the second quarter of 2013 to the same period of 2023.

Source: [https://www.morgancountycitizen.com/multimedia/slideshows/venture-capital-investments-have-skyrocketed-these-industries-have-felt-the-biggest-boost/collection\\_8feb8019-a237-5733-81f7-9e7973dd71a7.html#2](https://www.morgancountycitizen.com/multimedia/slideshows/venture-capital-investments-have-skyrocketed-these-industries-have-felt-the-biggest-boost/collection_8feb8019-a237-5733-81f7-9e7973dd71a7.html#2)

**125** How many pharma, biopharma, and contract research organizations are being surveyed by CluePoints in partnership with the Tufts Center for the Study of Drug Development on current risk-based quality management practices.

Source: <https://cluepoints.com/pioneering-ai-solutions-and-a-commitment-to-industry-wide-rbqm-advancement-secures-cluepoints-a-finalist-position-in-the-2023-scrip-awards/>

**21** The number of prioritized device guidance documents that the U.S. Food and Drug Administration's Center for Devices and Radiological Health intends to publish in fiscal year 2024—three of them as final guidances and 18 as draft guidances.

Source: <https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/cdrh-proposed-guidances-fiscal-year-2024fy2024>

**5** That number of startup healthcare companies that will participate in the 2023 accelerator program run by HeartX, a cardiovascular-focused healthcare accelerator that facilitates guaranteed hospital pilot projects and clinical trials for accomplished, early-stage companies bringing new cardiovascular innovations to market.

Source: <https://www.businesswire.com/news/home/20231016776811/en/HeartX-Accelerator-Announces-Five-Startup-Companies-Selected-for-the-2023-Program>



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