

# Clinical Researcher

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

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**Strategic Thinking for Complex Clinical Research Trials and Careers**

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## Clinical Researcher

### Association of Clinical Research Professionals

#### Managing Editor

Gary W. Cramer

[gcramer@acrpnet.org](mailto:gcramer@acrpnet.org)

(703) 258-3504

#### Director, Advertising & Exhibition Sales

Tammy B. Myers, CEM

[tammy.myers@acrpnet.org](mailto:tammy.myers@acrpnet.org)

(703) 254-8112

#### Media Kit

<https://acrpnet.org/advertising/>

For membership questions, contact ACRP at [support@acrpnet.org](mailto:support@acrpnet.org) or (703) 254-8100.

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<https://www.acrpnet.org/resources/clinical-researcher/> or e-mail [gcramer@acrpnet.org](mailto:gcramer@acrpnet.org).

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### Editorial Advisors for This Issue

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(Freelancer)

Staci Horvath, CCRA  
(Gradalis, Inc.)

Nadina Jose, MD  
(Rutgers, The State University of New Jersey)

Jerry Stein, PhD, ACRP-CP, ACRP-MDP, FACRP  
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PEER REVIEWED

## Unconventional Care: When Decentralized Research Models and Clinical Patient Management Collide

Elizabeth Anne Johnson, PhD, MS-CRM, RN; Lisa Marsh, MA, BSN, RN



Clinical trials are defined as the “testing of potential treatments in human volunteers to determine if drugs, medical devices, or biologics are safe and effective and should be approved for the general population.”<sup>{1}</sup> As we write this, more than 430,000 clinical trials are actively being conducted or have completed enrollment in the United States and 221 countries.<sup>{2}</sup> Each of these clinical trials is the rite of passage for a new treatment or therapy as it undergoes extensive safety evaluation, applicability for the intended population or disease

of interest, and demonstration of benefit compared to standard-of-care, in terms of approved drugs already integrated into patient care pathways.

In 2022 alone, the U.S. Food and Drug Administration (FDA) reported that 38,000 clinical trial participants enrolled in U.S.-based research, contributing to 50 new, approved therapies to be available for commercial use.<sup>{3}</sup> Each of these novel therapies, made possible through the volunteerism of trial participants, is the culmination of an average of 10 years of research and development.<sup>{4}</sup>

While traditional clinical trial models are conducted at a research site, such as a hospital or clinic, the acute phase of the COVID-19 pandemic brought in-person, non-essential interactions to an abrupt halt. Many hospitals were only allowing emergency admissions and critically necessary patient care, with most of clinical research activity not related to COVID-19 research placed on hold. Nurses belonging to specialty of nursing dedicated to clinical trial conduct, known as clinical research nurses (CRNs), were either furloughed, transitioned to inpatient care assignments, or tasked with adapting current clinical trials to remote or virtual means of completing participant safety assessments and investigational drug administration.<sup>{5}</sup>

This transition to what is known as a decentralized clinical trial (DCT) model involved new software platforms, use of video conferencing services like Zoom, and electronic consent and new ways to communicate with participants not setting foot in the facility. Even with clinical trial participation returning to in-person encounters for most research sites, the benefits of decentralized trials emerged as means to address longstanding issues in research. Decentralized trials permitted participants to remain in their communities, access local providers for care, and have research visits completed in the comfort of their home without potentially long and costly travel to far away research site. {6}

The DCT model extended the opportunity to receive cutting-edge investigational products to populations otherwise unable to shoulder the financial and commitment burdens of clinical trials, advancing the initiatives of equity and representativeness of diverse peoples in drug and device data. {7} The model is here to stay: faster-paced recruitment of participants and delivery of a better trial participation experience has equated to previously delayed trials becoming now viable for enrollment and more studies including remote components in the trial design. {8}

This paper describes the practice changes that CRNs, who perform direct patient care, may anticipate when DCT participation is involved, considering the CRN as a supportive role for clinical nurse care delivery guidance, identifying trial participants, and obtaining safety-related study information to inform care and ethical considerations. We also examine current trends in DCTs which affect clinical nurses.

### **Clinical Research Nurses: A Research Lifeline and Liaison**

A lack of clinical nurse awareness of clinical trial protocol–related restrictions on patient care could lead to medication errors, patient injury, or death. {9,10} For example, there are some experimental cancer therapies which interact with ondansetron, which is commonly administered for nausea. Instead, the clinical nurse may need to administer a different type of anti-nausea drug to deter widespread systemic drug interaction effects, which the research team could provide as part of information exchange while the patient is under a facility’s clinical care.

A recent literature review identified a need for clinical nurse education surrounding clinical trial conduct, an exploration of its tangent to patient advocacy in clinical settings, as well as establishment of effective communication with the study team and clinical leadership across the continuum of patient care. {11} To be clear, clinical nurses are not responsible for conduct of the clinical trial, however they benefit from an awareness of the patient's trial details at time of obtaining the medical history to provide the best possible patient care. For example, there may be dietary restrictions for patients on certain investigative medications or additional focused patient assessments integrated into the care plan.

The CRN is typically the primary site contact for other healthcare providers or research personnel for the clinical trial and serves as nurse educator for the clinical trial to direct care nurses and multidisciplinary medical teams. CRNs who specialize in clinical trial-related work may be based in the hospital setting and conduct in-services or training meetings surrounding particularly common touchpoints such as nursing assessment, medication administration, and signs/symptoms to monitor. The CRN is an expert in trial conduct and participant management and is a skilled communicator to providers and nurses outside the research team for best approaches to ensure patient safety and retention in clinical in-patient units or in external settings, such as affiliated outpatient clinics. {12}

The CRN works closely with the principal investigator (PI) of the trial and appraises the PI as to any change in participant status. Operating the local clinical trial logistics makes the CRN a trusted community partner and integral research team member, connecting the PI to nearby providers for continuing conversations surrounding intricate care management.

### **Decentralized Participant Safety When Standard-of-Care Becomes Not-So-Standard**

The flexibility in decentralized trial participation has generated high interest among cancer patients and patients associated with other diseases/disorders, with an estimated half of all patients being willing to enroll on a clinical trial. {7} For example, the number of oncology decentralized trials has risen 11% year-over-year, with almost half (46%) of all oncology trials including at least one component of remote or virtual-based participant management and/or data collection method. {8}

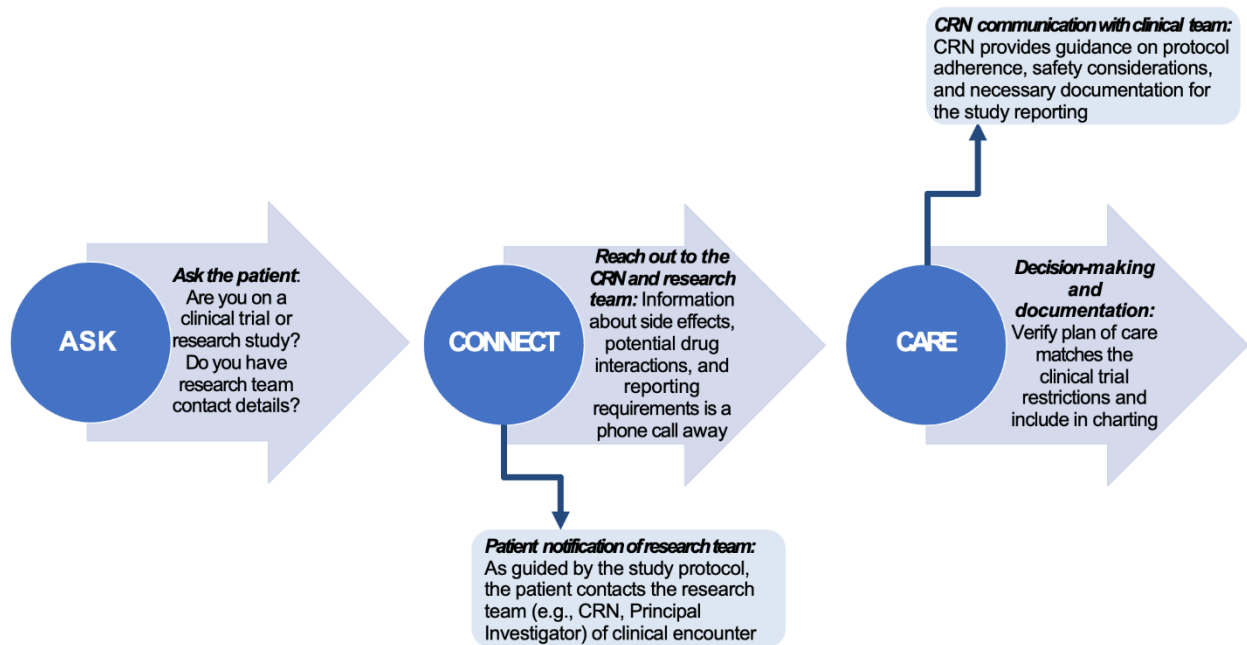
With more trial participants being able to remain in their home communities through the growth of decentralized trials, there is higher likelihood of clinical nurses to encounter patients who double as trial participants. However, clinical trial participants are easily camouflaged in the bustle of clinical tasks; wallet cards and other means of identification affiliated with the clinical trial are inconsistently implemented. {13} There is lack of reliable recall among participants to convey complex details surrounding what medications are safe for nurses to administer or which side effects are anticipated. {13,14} Further, electronic health record (EHR) systems are not standardized in their adoption for research-related use and may not include full integration with clinically facing modules. {14}

Safety-related details are necessary for the clinical nurse to navigate decision-making related to patient plan of care. Figure 1, derived from Hannawa’s essential communication framework and the Johnson, et al. clinical trial–specific communication framework, details steps to identify trial participants, obtain critical information, and interpret for clinical care actions. {15,16} Prompting each patient encounter with an inquiry such as, “are you participating in a clinical trial or research study?” initially identifies those patients requiring unique care considerations (ASK in Figure 1). Since a decentralized trial may mean the research team is not local to the facility caring for the trial participant, collecting research team details and initiating contact with the CRN will support education and guidance surrounding safe patient care (CONNECT in Figure 1). For example, many investigational drugs and devices may not have assigned names, being identified instead by alphanumeric identifiers that cannot be traced in common drug databases.

New technologies may be discovered, such as new remote patient monitoring devices or wearables. {6,17} What is considered standard-of-care may be incongruent to the clinical trial protocol. If not in adherence to the trial expectations, the participant may be withdrawn, resulting in loss of opportunity and access to potentially lifesaving products. There may be a period of “interactive sense making,” or trying to understand how the clinical trial is significant for patient care and what details are important based on input from the patient and the CRN. {15,18}

Documentation of clinical decision-making steps and fidelity of the care plan related to the trial protocol will support research team management of the participant. This includes dose adjustments or additional follow-up visits to monitor an adverse event (CARE in Figure 1).

**Figure 1: Recommended Steps for Clinical Management of a Patient Participating in a Decentralized Trial**



CRNs may support clinical nurses through other modalities of obtaining clinical trial information important to care delivery, such as tipsheets or binders of key details left at nurse stations. Some facilities may use special icons, different colored chart flags, or wristbands to help clinical nurses and other healthcare providers distinguish clinical trial participants from “regular” patients at the facility. {17}

Clinical nurses are recommended to be watchful for dashboard notifications in the EHR and corresponding research-related modules that may require review so that medications, assessments, and frequency of patient status checks are aligned to the type of clinical trial and alterations to normal laboratory values—for example, due to an investigational drug or device.

### **Implementation Considerations**

Decentralized trials expand trial access to settings outside traditional hospital or research units, which comes with a unique set of ethical challenges related to institutional review board (IRB)



review and PI oversight. During the COVID-19 pandemic, decentralized trial models or a mix of traditional (at a facility) and some decentralized (such as blood draws at home) activities were encouraged to continue participant access to novel treatments while adhering to federal guidelines for minimizing interpersonal contact.{19}

In 2021, the FDA issued guidance on how to navigate regulatory hurdles without the structure of organizational bounds of a hospital. Per the guidance, a research team is delegated to ensure safety of participants in the decentralized model in collaboration with their respective IRB to support contextual adaptations to how to control for varied resources in home-based or community research conduct.{20}

Decentralized trials require close partnership with participants, caregivers, and clinical providers to minimize risk or potential for harm.{21} Partnership includes PI oversight of local provider engagement strategies and communication channels, which includes the CRN as the backbone and liaison for the community and participant. Effective communication between clinical nurses and CRNs supports participant safety and quality in recorded outcome data, which supports new drug and device applications to be approved for commercial use.

### **Informed Consent, Ethical Challenges, and Communicating Safety Information**

While the PI, CRN, and research team are ultimately responsible for supporting communication of clinical trial participant safety information to clinical teams, the clinical nurse holds a critical role in advocating for safe care aligned, when possible, to the research protocol. Per the American Nurses Association Scope and Standards of Practice published in 2021, Ethics Provisions 2 and 3, the nurse's primary commitment is to the patient which includes promotion for health and safety. Standard 10 notes that the nurse must also be able to effectively communicate across all areas of practice which includes ancillary medical teams as well as the patient.{22}

Communication is the cornerstone to quality patient care, and poor or ineffective communication between research and clinical teams may result in harm to participants and stress for the clinical nurse.{23} An ethical challenge pertaining to communication of safety information is the informed consent process and how best to support participant understanding of protocol

expectations, when to communicate their involvement in a clinical trial to the clinical nurse, and how informed consent affects clinical nursing practice. Particularly when not accustomed to integrating research-related safety considerations in the clinical setting, nurses have reported distress when trying to manage an adverse event and the extra work of unique care requirements with a participant. {24}

Meanwhile, participants historically have been generalized as having significant challenges understanding trial material presented within informed consent forms, which can be at a 10th-grade reading level and confusing due to detailed information presented in scientific terminology. {10} Tam, et al. reported across 103 studies and 135 cohorts of trial participants that only 54.9% could name at least one risk associated with participation on the clinical trial. {25} While wallet cards are commonly associated with clinical trial communication of safety and contact information to clinical teams, Schoenenberger-Arnaiz, et al. found that, across 67 protocols, 37% did not mention the card or its use in the event of clinical care within the informed consent form. {13}

When confronted with ethical challenges such as those with balancing integration of trial safety information within clinical care workflow, clinical nurses have reported that support from colleagues, such as CRNs, aids in the navigation of clinical decision-making. Clinical nurses have also reported a sense of pressure and feeling inadequately informed or trained to manage clinical trial participants as patients, which is compounded with communication gaps and participant knowledge deficits. Routine engagement with CRNs and details pertaining to the informed consent form and the process of consent were additional supportive structures to aid clinical nurses in feeling more prepared during encounters with trial participants. {24}

The CRN, PI, and other members of the research team are delegated by a trial sponsor to support ethical and optimal trial conduct. This delegation and responsibility then translate to ensuring that clinical nurses feel supported in managing participant care outside the study. Research team actions can include simplification of informed consent form language for participant understanding as well as education in-services for nursing staff of hospital systems pertaining to trial participant clinical management strategies. {10,25}

## **On the Horizon: Future Trends in Decentralized, Remote Research**

The influx of localized participation in clinical trials and research studies has sparked integration of research-related services among companies with pre-established presence in metropolitan and non-metropolitan settings. Following the acute phase of the COVID-19 pandemic, healthcare titans CVS Health and Walgreens announced a strategic focus on clinical trial participant recruitment via their pharmacy and clinic locations, leveraging the existing brick-and-mortar community footprint and customer traffic to create awareness of decentralized trial opportunities. Both companies communicated their commitment to address a common issue of DCTs surrounding investigational product management, which is the shipping, storage, and dispersal of experimental drugs in the event the local research site does not have the necessary resources. {26,27}

As almost 4 out of 5 Americans live near a Walgreens, there is high potential for more diverse, representative enrollment of trial participants, lending enhanced real-world data to inform new drug and device application reviews prior to FDA approval. {27,28} While CVS Health will depart the decentralized trial space by 2024, Walgreens and other healthcare or pharmacy-based companies have retained their resolve to support remote participant trial recruitment through expanding their programs into primary care settings, urgent care, and retail locations. {29}

The quest for diverse patient population representativeness in clinical trial data includes geographic diversity, which includes the enrollment of suburban or rural-dwelling residents to better understand the pragmatic, more logistical aspects of a novel drug or device's use in areas which are lacking in terms of healthcare resources.

In October 2022, Walmart announced that it too was entering the clinical research space, with a focus on increasing access to clinical trials and heavy adoption of mobile, virtual technologies (such as a mobile app) to pair pharmacy and clinic patients to trial opportunities corresponding to their health information. {30} Retailer Dollar General also is leveraging its heavy presence in rural areas, launching thousands of pilot mobile clinics in some stores as part of its healthcare debut. {31} The staffed mobile clinics, called DocGo On-Demand, signal an overarching change

in community-focused healthcare delivery, broadening of consumer healthcare options, and potential access points of decentralized trial patients outside hospital-based facilities.

As these retail and commercial locations are found across both urban and non-urban centers, they provide potential job opportunities for CRNs given their specialization and expertise. The inclusion of non-traditional study sites also may be integrated as resources to facilitate trial procedures (e.g., specimen collection, physical assessments, or investigational product dispensing) closer to the participant's location, which may create workflow efficiencies for CRNs in visit scheduling and staff allocation.

Nurses working in suburban and rural community clinics, or in freestanding emergency/urgent care facilities, may be contributing to the conduct of clinical research in cases when DCT participants require care or completion of procedures outside the research setting. For example, a participant may experience a side effect or critical symptom requiring medical attention. Having a clinical nurse attuned to assessing for trial participation in a non-hospital setting benefits the patient to ensure safe care congruent to the protocol restrictions. The clinical nurse may then also contact the CRN of the research study for more information related to adaptations to nursing assessments and explanations of signs or symptoms attributable to the study drug or commonly seen on the trial.

Particularly in lower resourced settings, such as critical access hospitals, clinical nurses will benefit from quick touchpoints with a CRN on how to adapt complex investigative product management within the constraints of the extend of care traditionally provided. For example, the CRN may work with the clinical nurse on an interfacility transfer with documentation to a hospital with critical care capacity should a participant require a higher degree of supportive care.

## **Conclusion**

In a recent survey of clinical research executives, almost 4 out of 5 noted use of a decentralized trial model within the next year as part of the development pathway of a new drug or device toward commercialization.<sup>{8}</sup> DCTs are here to stay, with potential to increase clinical trial access, diversity, and likely faster approval of new treatments.

As clinical trial participation becomes more mobile and accessible outside traditional research centers, nursing awareness of the unique care considerations of patient-participants becomes crucial. While clinical trial details are not readily available at point of care for many nurses, adjusting patient interviewing and adopting a situational awareness to the potential of encountering a trial participant (see Figure 1) can keep a community member taking an investigational product safe. CRNs are at-the-ready as skilled communicators of critical safety and reporting information in such situations, balancing clinical experience with trial expertise to assist clinical nurses in care decision-making.

For many patients, each clinical trial enrollment is a hard-fought opportunity to keep hope alive when other treatments are not effective. Widening trial access and closing the barrier gap among under-represented populations prompts agility across the nursing profession to extend patient advocacy to those enrolled in clinical trials. Creating a flexibility in the definition of standard-of-care beyond established treatments incorporates experimental treatments deemed appropriate for a patient's particular disease process, disorder, or symptom. Made possible by decentralized trials, cutting-edge medicinal advancement has never been closer to home.

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**Elizabeth Anne Johnson, PhD, MS-CRM, RN,** ([elizabeth.johnson37@montana.edu](mailto:elizabeth.johnson37@montana.edu)) is an Assistant Professor in the College of Nursing and Co-Director of the Biomedical Innovation for Research and Development (BioReD) Hub at Montana State University.



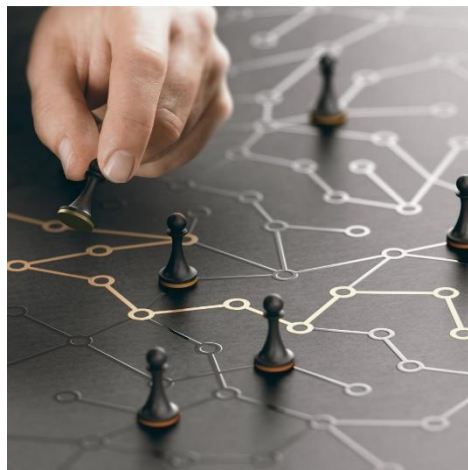
**Lisa Marsh, MA, BSN, RN,** ([lisa.marsh@northwestu.edu](mailto:lisa.marsh@northwestu.edu)) is a member of the Adjunct Faculty for the Northwest University Mark and Huldah Buntain College of Nursing, a Committee Member of the International Association of Clinical Research Nurses, and a Clinical Trial Lead with Boehringer Ingelheim.



PEER REVIEWED

## Professional Development of an Independent Consultant in Clinical Research

Steven Eric Ceh, DPM



Becoming an independent consultant in clinical research requires taking a number of steps and dwelling on several considerations. This article provides a comprehensive look at professional development interwoven with my own experience working in clinical research as an independent consultant/contractor, including how I (and others) entered the profession, built and maintained my experience base, and launched my own LLC, along with my perspectives on professional development as it relates to clinical research.

### Getting into Clinical Research

The pathways toward a career in clinical research are varied. First, there are professional degrees such as PhD or MD, the training for which intentionally leads toward a career as a medical scientist working in drug and device development. The U.S. Bureau of Labor and Statistics recognizes this occupation and has detailed description on how to pursue it listed in its Handbook. However, this and related jobs are not directly connected to working with research participants. For example, if you search the same database for any sign of entries for “clinical research investigator/principal investigator (PI),” “clinical research associate (CRA),” or “clinical research coordinator (CRC),” you will be out of luck.

While an investigator is usually a medical doctor, apart from some licensing requirements for certain aspects of a CRC’s duties, there are no formal prerequisite degrees for them or for a clinical CRA.

While this affords flexibility and diversity on becoming a CRC or a CRA, it may require more effort in creating one’s professional path. It also leads to some fantastic stories on how individuals began their work in clinical research.

My journey in clinical research began in the early 1990s. While reading the local newspaper in Austin, Texas, I came across an article on the pharmaceutical industry and wondered if my background in podiatric medicine was relevant to the profession discussed. I made an appointment and visited a local contract research organization (CRO) to speak with several of its employees. I was able to meet a dentist who had transitioned to become a CRA and felt that I could do the same. Several months later, I interviewed for a position and became a CRA.

Later CRO and pharmaceutical company jobs that I held in research came from directly reaching out to their Human Resource departments to discuss employment options. Some of these transitions were motivated by discussions with other research professionals in related fields.

## **Tales of the Unexpected**

### *The Investigator*

An investigator colleague of mine started as a dual major in Pharmacy and Pre-Med. Shortly after completing his residency in Internal Medicine 35 years ago, he became a PI while continuing his medical practice. He served on many hospital committees and taught hospital-based clinical medicine for the local Medical School. More studies and opportunities followed, including working as medical director of a CRO. Eventually, he moved toward full-time clinical research and connected with research colleagues at ACRP, even serving on the Association's Certified Principal Investigator (CPI) Exam Committee. He joined ACRP's Association Board of Trustees while continuing to publish and assist with developing training programs and teaching.

### *The CRCs*

I know a CRC who got into research because it was one of the few jobs she could get with a Master of Health Services Administration. Another CRC said a neighbor asked her if she was afraid of drawing blood and wouldn't mind helping him with his clinic on weekends; that grew into a full-time study coordinator position.

## *The Project Manager*

A project manager of my acquaintance was a young night shift ICU nurse with no social life who was thinking of going to nurse anesthetist school when a friend suggested she apply for a day job at a pharmaceutical company compiling safety reports during the fen-phen crisis. After completing that job, her interest shifted toward clinical research, where she got a job as a CRA. Her management skills became apparent during her four years as a CRA, enabling her to transition into a project management job. Continued success and experience followed, allowing her to move into Clinical Operations Director positions and now service as a Vice President of Operations.

## **Pathways for the Planned and Prudent**

A career in clinical research guided by fate or luck may be of historical interest; however, there are now many curriculums designed for students in the early stages of a career in clinical research and for more experienced individuals such as investigators, coordinators, and sponsor representatives who want to expand their knowledge and skills in the field. These include the following programs:

- Internships{1}
- Bachelor of Science in Clinical Research{2}
- Master of Science in Clinical Research{3,4} (Some Master of Clinical Research programs are offered entirely online.)
- Certificate in Clinical Research{4}
- Post Graduate Diploma in Clinical Research{4}

## **Professional Development**

Professional development involves learning to earn and then maintain academic and professional credentials through formal coursework, conferences, and informal learning opportunities situated in practice. It has been described as intensive and collaborative, ideally incorporating an evaluative stage.{5} There are various approaches to professional development, including

consultation, coaching, communities of practice, lesson study, mentoring, reflective supervision, and technical assistance.{6}

Individuals may participate in professional development because of an interest in lifelong learning, a sense of moral obligation, and goals for maintaining and improving professional competence by enhancing career progression, keeping abreast of new technology and practices, or complying with professional regulatory requirements.{7,8} This may lead to advancement or change in job, or simply to doing better in a current position. Examples of professional development include college studies, online training programs, industry certifications, coaching, mentoring, and consultation, the intents of which in a clinical research context may be to enhance a worker's ability to practice safely and effectively and/or to improve medical knowledge and skills in such areas as management, team building, professionalism, interpersonal communication, technology, teaching, and accountability.

### **Strategies for Professional Development**

A central theme to research documentation is “If you didn’t write it down, it didn’t happen,” but when it comes to planning your professional development, perhaps that should be rephrased as “If you don’t write it down, it won’t happen.” Writing things down enables a higher level of thinking. It allows you the freedom to focus on actions to accomplish your goals; imagine building a house without plans.

According to a study done by Dr. Gail Matthews at the Dominican University in California,{9} you are 42% more likely to achieve your goals just by writing them down and sharing them with a friend. Writing things down makes them real and signals your brain that you’re serious about making them happen and increases your sense of commitment. A Harvard Business Study found that people with written goals are three times more successful than those who don't write down goals.{10}

When I started in clinical research as a CRA, I wrote a very basic professional work plan that included milestones for learning regulations and guidelines (see below), gaining experience in the position whereby I deemed myself competent, and securing several reliable references; completing the CRA certification exam also was a goal before considering embarking on an

independent consultant role. Maintaining your competency in your various working roles should always be included in your plan.

## **Steps to Becoming an Independent Consultant Contractor**

For the sake of this article, an independent consultant in clinical research would be an individual working on a contractual basis in the role(s) in industry such as a monitor, study coordinator, project manager, medical writer, statistician, data technician, regulatory specialist, quality assurance auditor, etc. A hybrid role is possible based on your experience level when you decide to work as an independent contractor. For example, a well-experienced CRA could also have the ability to perform a site audit and/or prepare one for an audit.

### *1. Develop, maintain, and advance your knowledge and experience level.*

A significant part of one's development is tied to learning and maintaining the knowledge and skillsets of a desired profession. Core knowledge items include industry regulations, accompanying guidances, { 11 } and Good Clinical Practice (GCP) references. { 12 } In addition, a good understanding of the results of regulatory inspections such as those found on the FDA website { 13 } fosters habits for avoiding punitive actions.

I began by learning all the relevant FDA regulations and guidance documents. Then, when I started my actual work, I kept an "A-to-Z file" in which I sorted and filed the various forms, reports, processes, and solutions that helped me conduct my CRA work. I was amazed by how compiling this file made it easier for me to organize my thoughts, remember the information better, refer to it when I needed help, and provide substantive insight at team meetings.

A recommended knowledge base list for clinical research professionals includes the following:

- Title 21 *Code of Federal Regulations* (CFR) Parts 11, 50, 54, 56, 312, 314, 812, 814 and Title 45 CFR Part 46 (The Common Rule) (<https://www.archives.gov/federal-register/cfr>)
- The Belmont Report (<https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html>)
- International Council for Harmonization GCP Guidelines E6(R2), E2A, E8 (<https://www.ich.org/>)

- FDA Information Sheets and Guidances on such matters as FAQ on Clinical Research, Guide to Informed Consent, Recruiting Study Subjects, Pre-Study Screening Tests, Foreign Clinical Studies for U.S. Submission, Drug Study Designs, Sponsor-Investigator-Institutional Review Board (IRB) Relationship, FDA Inspections of IRBs and Investigators (<https://www.fda.gov/industry/fda-basics-industry/guidances>)
- FDA GCP Inquiries (<https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/good-clinical-practice-inquiries>)
- Industry literature such as articles from *Clinical Researcher*, *Journal of Clinical Research Best Practices*, *SOCRA Source*

In conjunction with the start of your work, it is also important to consider establishing a mentor, a role model to ask questions/shadow, a network of peers, and study groups. There are a variety of services which focus, at least in part, on connecting similar people to one another in the same industry, such as Job Share Connect, Skout, and Meetup. These can help you progress in your career and may be the foundation for subsequent steps.

A certification goal in your area of expertise is an excellent addition to your written professional plan. Preparing for certification can strengthen areas of weakness and make you better at your job. {14} Certification is a surrogate for quality and recognition for your accomplishments.

## 2. *Form a company (i.e., LLC or S corporation).*

Once I felt that I had an adequate competency level as a CRA, which was after seven years in the industry working at a CRO and pharmaceutical company, and having a number of personal references for networking, I decided to explore becoming an independent consultant. I would be remiss if I did not strongly advise taking your time to carefully consider this option, insofar as the pros/cons of being a consultant contractor and thinking through and writing a business plan for marketing yourself, identifying clients, and negotiating a contract. {15}

Certainly, timing is important in launching your career as an independent consultant. With that, I was fortunate enough to know someone who needed a full-time contract CRA, which enabled the transition to be easier...for me. Some choose to start with part-time availability or to service several contracts at once. How you launch yourself as a consultant should be ultimately prefaced on your comfort level and personal family situation.

For small business owners or sole proprietors, an LLC is often the easiest and most cost-effective way to incorporate. If you're a sole proprietor, it might be best to establish an LLC since your business assets are separated from your personal assets. You can always change the structure later or create a new company that's an S corporation. An S corporation would be better for more complex companies with many people involved, since there needs to be a board of directors, a maximum of 100 shareholders, and more regulatory requirements. {16}

In my case, I opted to create an LLC and had a local lawyer assist with the paperwork and filing. The cost was several hundred dollars. Another option to create your LLC is to use a legal entity via the web, such as Legal Zoom.

Once I decided to transition to an independent consultant role and established my LLC, I updated my written professional plan to include writing one or more articles for an industry journal, to speak at a large conference, to volunteer in some way, and to teach others in the industry as opportunities arose. Maintaining your competency in your various roles as an independent consultant is inherent in your plan.

### *3. Establish a business bank account.*

You want to create a business bank account so that the transactions of your business are transparent, separate, and not co-mingled with personal actions. I chose a local bank which I could physically visit or mail documents to.

### *4. Secure business credit card(s).*

It is strongly recommended that you have at least one credit card dedicated to your business; it doesn't have to be a "business" credit card just so long as it is strictly used for your business, thereby avoiding co-mingling of business and personal information. Many contractors opt to use a card with a cashback option—particularly with a higher rate for travel transactions, since a majority of your business credit card purchases will be in the realm of airline tickets, hotels, and restaurants.

*5. Obtain state licensing.*

You will need to find out what documents, such as licensing, need to be completed for the State your company is based in. Also confirm if there are requirements for annual reports or other filings.

*6. Obtain E&O insurance.*

Most of your prospective clients will require that you maintain a certain level of E&O (errors and omissions) insurance as a self-employed professional, and this can come from a number of available sources.

*7. Obtain healthcare insurance.*

The largest potential expense for an independent consultant is healthcare insurance. If your spouse or partner has an option for you to be covered, that will probably save you a lot of money. Otherwise, you need to contact a healthcare vendor to identify the best coverage policy for you. If you happen to be a veteran, the VA Medical system is certainly an option for your healthcare needs.

*8. Take care of quarterly taxes.*

As a consultant, you will most likely need to set up paying of quarterly taxes, since you will probably be paid as a 1099 employee. I recommend that you meet with a tax preparer and/or accountant to discuss this and the running of your business. This individual should be able to provide guidance on options for operation of your business (i.e., bookkeeping services or mechanisms for you to do all or some of the related tasks). In my case, there was a SCORE (Service Corps of Retired Executives) program in my area which holds meetings to assist small business owners establish and grow their business. I was able to develop my own forms to keep track of income, expenses, and other information necessary to file required reports and complete my income tax forms.



### *9. Set up a SEP-IRA.*

As a consultant, you have the option of setting up a SEP-IRA in which you can fund up to 25% of your compensation. Your accountant or tax preparer can assist with setting up this type of account.

### *10. Don't forget the time/expense bookkeeping.*

As indicated above, as a consultant, you will need to keep track of information related to your business; you can employ someone or do some or all of it yourself. I chose to meet with an accountant/tax preparer who provided me with the necessary information to develop my own files to keep the time, expense, and other related information necessary for him to prepare my taxes as well as have in case of an audit. I gradually learned to prepare my own tax returns.

### *11. Attend to other files (summary, mileage, invoice receipt/payment, etc.).*

Besides the basic files related to documentation of your expenses and time, there are other documents which facilitate the preparation of your taxes and provide information on your business, in general. Again, these files were the result of meeting with an accountant/tax preparer and involved such things as a mileage and utilities log (if using your home as office space), insurance payment information, tracking invoice for submission and receipt of client payments, income log, healthcare payment log, real estate tax payment log, etc.

### *12. Equipment*

Basic equipment needed by a contractor would include a file cabinet/fire-safe storage, phone, computer with basic software, backup drive, internet and video conference capabilities, and a multipurpose machine (i.e., print, copy, fax, scan). You can create a business e-mail address by adding an account to your existing e-mail provider. If you set up an office in your home, you should make that space totally dedicated to your business purposes.

## Working as an Independent Consultant Contractor

Once you begin your first contract as an independent consultant, chances are that, if you work hard and do a good job, you will be offered repeat business. As well as focusing on your contracted job, it doesn't hurt to speak up if you see something that would help the company with its projects. Networking with a couple other contractors also can lead to work, especially when they have a contract which needs additional personnel. Social media sites such as LinkedIn can offer another means of networking to find work. Maintaining ties with a couple of professional recruiters who offer good hourly rates for your work should be considered as well. However, whenever you can contact a company directly and negotiate a contract with it, this will usually result in the best compensation rate.

Traveling, and your willingness and ability to do so, will have a major impact on your potential revenue. I have a few specific recommendations in that regard:

- I used carry-on luggage whenever possible; that saved me a lot of time on both ends of my trips.
- Pack wisely and efficiently. I kept a separate toiletry bag to facilitate packing. I always brought a sweater or light jacket for use as a needed comfort *en route* or onsite.
- Eat smart. Get to know what works for you when traveling (i.e., timing and amounts of meals, fluids, and snacks). Remember, you don't have to eat or drink the full, allotted daily allowance; pace yourself.
- Make provisions for exercise either at a gym in or near the hotel or walking in the area. I always liked when it was possible to walk to and from a site from my hotel. Maintaining your stamina facilitates your ability to travel and work as a consultant.

Continue to grow your professional network; begin to shadow inspiring mentors in desired advanced positions. Consider starting a journal club<sup>{17}</sup> and keeping a reference file that includes various questions/answers from your industry journals.

There are myriad other resources to maintain your knowledge about the clinical research enterprise and the overall life sciences industry, including <https://about.citiprogram.org>, CenterWatch, Barnett International, and <https://www.mycme.com>.

Continue to maintain competency; however, your training should now involve modes which go beyond GCP knowledge to include real-life situations. Use of online Continuing Medical Education programs with guest lecturers is also useful to keep abreast of changes in your disease condition(s) area of expertise.

Seeking advice from a mentor is possibly more important as you advance in your career to assist you in pursuing the job that is the best fit for your experience and personal status. Working with mentors is a proven method for achieving next-level goals. {18} One should also consider having a critical friend. A critical friend is a trusted person who asks provocative questions, provides data to be examined through another lens, and offers critique of a person's work as a friend (e.g., a CRA helping another CRA). A critical friend takes the time to fully understand the context of the work presented and the outcomes that the person or group is working toward. The friend is an advocate for the success of that work. {19}

Any activity that involves advancing your career should include a review (and update) of your professional written plan, accordingly.

### **Giving Back (or Paying Forward) to Advance the Industry**

Not enough attention in clinical research has been paid to giving back and growing the profession. Once you become experienced and competent in your professional career, you should consider doing something in that regard to advance the profession. Here are my suggestions:

- Write journal article(s) and develop other publications (training manuals, monitoring guides, etc.)—Quite often, the industry moves forward by those who put forth standards and ideas. Examples of popular journals for clinical research personnel include *Clinical Researcher*, *Journal of Clinical Research Best Practices*, *Journal of Clinical Investigation*, *SOCRA Source*, and *Journal of Medical Devices*.
- Volunteer—Many people overlook volunteering and miss out on meeting new people, learning and doing different things, and thereby expanding their reach in the process. Teach the public what our efforts to increase its involvement in trials are really all about.

Consider giving a presentation on clinical research in your community, speaking at your child's school, or presenting to undergrads at your college.

- Present at an industry meeting—Use your work experiences as a basis to present at a professional association's national or regional conference, or at one of its chapter's meetings in your area.
- Teach/mentor a new colleague—This would add a dimension to your current position and could blossom into a new aspect of your career. Some individuals have certainly parlayed this opportunity into writing blogs and presenting topics in podcasts.

Personally, I was able to write a number of articles which were published in industry journals and speak at a large conference. I had the opportunity to get involved with several committees and served for 20 years. While working on several contracts, I was able to conduct training sessions on monitoring strategies and mentor new CRAs. So, all of these things are possible; you just need to be open to the opportunities that arise, and while volunteering may sound like a hit on your income, the rewards from the experience far outweigh the non-billable time involved.

## **Conclusion**

This article has provided insight into various ways the clinical research profession may continue to further develop and advance interwoven with suggestions on breaking out as an independent consultant. Avenues for entry, methods to learn, train, and persist were outlined. Examples of routes for giving back provide current members of the profession ways to help further define and propel it into the future.

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**Steven Eric Ceh, DPM**, ([sec\\_consulting@sbcglobal.net](mailto:sec_consulting@sbcglobal.net)) is a Consultant with SEC Clinical Consulting, Ltd. In Westerville, Ohio.

## Data Monitoring and Complex Clinical Trials: Toward a Solution

Professor Deborah Ashby, MSc, PhD; Professor Jennifer Visser-Rogers, MSc, PhD



Complex trial designs may be more efficient than the traditional two-group model, but they also present important data monitoring challenges.

Standard one-size-fits-all approaches to evaluating accumulating data are not feasible when working with multiple variables, whether they be multiple endpoints, multiple treatments, or both. Ensuring a robust framework upon which to base stop/go calculations is essential to protecting participant safety whilst accelerating access to life-changing new treatments. The weight of responsibility carried by data monitoring committees (DMCs) is not insignificant, so it is important that these complexities are worked through.

### Background

DMCs are a crucial element of clinical trial conduct. These committees confidentially review data as they accrue, to monitor primarily for safety (and often efficacy) to inform continuous stop/go decisions. This is particularly important when we consider the staggered nature of clinical trial recruitment—many studies will still be enrolling when data on early participants become available. DMC review can reduce the risk of additional patients being exposed to serious adverse events or toxicity, or speed up access to treatments that show efficacy. These independent panels also ensure the continuing validity and scientific merit of the trial. Statisticians are an integral part of this process.

However, the emergence of more complex trials, such as platform trials and those with multiple endpoints, complicate the work of DMCs. One-size-fits-all statistical methods are no longer valid. Instead, researchers must employ a much more nuanced approach that considers a variety of factors, including the research question, therapy area, and patient preferences.

## **An Emerging Landscape**

For decades, clinical research has been based on a standard two-group, singular endpoint methodology. This robust methodology has served healthcare well, but it is also slow and inefficient. It can take decades to bring a new drug candidate through clinical development and onto market, and more investigational products fail than succeed.

As such, new ways of working are emerging. They include seamless phase trials, interim analyses, as well as more innovative designs such as platform trials, which allow new interventions to be added, assessed, and removed (either for efficacy or futility) as data accumulate. While such models, which can significantly accelerate development, are not new, they have become much more widely used since 2020, when they were used to investigate treatments during the COVID-19 pandemic.

PRINCIPLE, REMAP-CAP, and RECOVERY are among the successful UK-based platform trials that were initiated early in the COVID-19 pandemic, each testing multiple potential treatments for the virus. Through this efficient design, the in-hospital RECOVERY trial, for example, was able to demonstrate the efficacy of agents such as dexamethasone and tocilizumab within months of study set up. Others, including a study of hydroxychloroquine, were stopped early due to futility. These experiences showed that innovative trial design can deliver access to efficacious treatments quickly and safely, while also limiting the time and resources spent on clinical dead ends.

While the potential benefits of these designs are clear, they complicate the nature of DMC assessments, which remain the bedrock of making such stop/go decisions. Complex clinical trials provide opportunities, but the question of how best to manage data monitoring for these studies remains. Some of the issues have been thought through, but there are still outstanding questions that are not easy to answer.



## Models and Challenges

Multiple endpoints can arise in treatment trials but are more frequently associated with prevention studies, where a treatment may prevent the condition for which it is intended but increase the risk of other health considerations. Teams will need to balance these different endpoints, considering trade-offs and weighting for their stop/go strategies. A clinical trial for trastuzumab in women with non-metastatic, operable primary invasive breast cancer, for example, showed a reduction in the proportion with either disease progression or death but an increase in cardiotoxicity. This is, in fact, a common problem for many oncology drugs, so how should one proceed?

Numbers needed to treat and numbers needed to harm are a common way to quantify these increases in benefit and risk, but sometimes it is more nuanced and requires human thought alongside the numbers. These approaches assume that one cares equally about breast cancer recurrence and cardiotoxicity, which may not be the case. Furthermore, cardiotoxicity is easy to treat if you are looking for it, so by being a known risk factor associated with oncology drugs, in a way, decreases its realized risk.

Patients themselves will also have differing viewpoints on tolerability. Hormone replacement therapy (HRT) is known to affect, for example, cardiovascular risk, colon cancer risk, endometrial cancer risk, and chances of hip fracture. How should all these risks (and more) be weighed up? It's important to look at not just these side effects, but also symptoms of the menopause itself and personal preferences. Women with highly bothersome menopause symptoms will have a higher threshold for HRT side effects than those who are asymptomatic. Such considerations are challenging to translate into statistics, but decision aids and visualisations can help individual women make their own treatment decisions. The difficulty for DMCs is making decisions at a clinical trial level; they cannot make decisions for individual women—they either stop the trial or they don't stop the trial.

Working with multiple treatments can be equally as challenging. While factorial designs are useful when all the treatments are known in advance and will be used in the same group of people, they are not helpful when not all interventions are known up front, as was the case during the COVID-19 pandemic. In this scenario, fully adaptive platform trials are extremely powerful. They are representative of the evolution of scientific learning but create issues in terms of running the trials and DMC considerations.

The community care-based PRINCIPLE trial, for example, evaluated eight treatments and interventions using an adaptive Bayesian “find the winner” model. It also used a response-adaptive randomization, which favored the treatment that was doing best. Via regular DMC review, the evaluation of hydroxychloroquine was stopped due to futility in May 2020, and azithromycin and doxycycline were stopped in January 2021. Inhaled budesonide was found to be beneficial and rolled out for routine use in April 2021.

Despite its immense success, this trial was not without DMC challenges, some of them being all the more relevant in terms of best practices for trial conduct during a pandemic. For example, accounting for changes with the control group from non-vaccinated to vaccinated status whilst the trial is ongoing. Bayesian time-machine models can help with this but are heavily dependent on modelling and their associated assumptions, so sensitivity analyses are important.

Other difficult questions involve how long a patient should be randomized to a treatment when early data suggest that it is not effective. In a pandemic situation especially, where media interest is high, these decisions can be influenced by publicized assumptions about treatment efficacy or other trials and observational studies which might sway opinions about treatment.

How should DMCs for different trials interact with each other and what information should be shared? Further, how much data on completed treatments can be published while a study is still ongoing? Sharing too many results whilst the trial is still ongoing could reveal information on a trial’s current status, and it is difficult to reveal full details on a control group whilst it is still being used as a comparator for other treatments. How to balance these issues against transparent decision making is a difficult decision.

### **Answered and Unanswered Questions**

It is clear that questions around the most effective, robust data monitoring processes for complex clinical trials remain, and there is much need for further debate and framework development.

However, what we have learnt so far is that the DMCs cannot work in silos, and that approaches must often be designed on a case-by-case basis. There is no one-size-fits-all for complex trial designs and experts must work together to answer outstanding questions. Solutions need to be flexible, start with a

shared understanding of the trial’s purpose, and be based on a clear understanding of the decision guidance (which should be determined before any interesting data have been seen) as well as its implications.

Decisions around weighting and trade-offs are often informed by patient preferences and lived experience. As such, there is a huge need for researchers to work closely with the people they are setting out to serve from the earliest possible point in development.

The consequences of getting this wrong—either by allowing trials to continue when they are doing harm, or by incorrectly halting a study of an efficacious treatment—are too significant to ignore. Importantly, statisticians, who tend to be a lone voice on DMCs, need to be able to communicate their methods, calculations, and the implications of their work to the wider panel. Complex clinical trials can be hard to understand, but it’s vital that statisticians help their clinical colleagues navigate this new landscape.

## **Conclusion**

Complex trials hold huge potential. They are more efficient, they deliver answers quicker, and they are less expensive to conduct. If we are to seize this opportunity, we need to be prepared.

It is true that there is much work to be done, but it is incumbent on statisticians to ensure that their methodology is in order and in place if these emerging clinical trial models are to deliver on their promises.



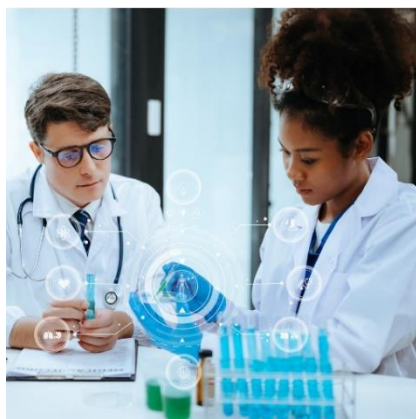
**Professor Deborah Ashby, MSc, PhD**, is Interim Dean of the Faculty of Medicine at Imperial College London where she holds the Chair in Medical Statistics and Clinical Trials.



**Professor Jennifer Visser-Rogers, MSc, PhD**, is Vice President, Statistical Research and Consultancy, with Phastar.

## Realizing New Miracles: Gene Therapy Trends in 2024 and Beyond

Dr. Jörg Schneider



Cell and gene therapies have been life-changing for many patients. As U.S. Food and Drug Administration (FDA) Center for Biologics Evaluation and Research Director Peter Marks, MD, PhD, said at a Cell & Gene Meeting on the Mesa last year: “We may not believe in miracles. But there are things that are miraculous, and this is one. We want to ensure that we get it right with smaller populations, but then hopefully see this grow to bring the benefits of cell and gene therapy to larger populations. We’ll use all the tools in our toolbox to help make that happen.”{1}

There are many reasons to be excited about the field of advanced medicinal therapeutic products or cell and gene therapies. There are, however, also issues with these products. A recent paper highlighted the disproportionate rise in FDA clinical holds for cell and gene products as compared to small molecules, most commonly due to an adverse event or patient death.{2}

Trends in the near-term will focus on ways to address current limitations, be those due to safety, immunogenicity issues, targeting challenges, dosing issues, or regulatory and payer barriers. The article explores four areas of focus for the year ahead.

### Adeno-Associated Virus (AAV) Gene Therapy

As one of the most mature gene therapy technologies, AAV remains the dominant gene delivery vehicle. In recent years, several gene therapies using an AAV vector have received regulatory approval for a variety of rare diseases with unmet medical needs (see below).

Name	Year of Approval	Indication	AAV Type	Route of Administration
Luxturna	2017	RPE65-mutation-associated retinal dystrophy	AAV2	Subretinal infusion
Zolgensma	2019	Certain types of spinal muscular atrophy (SMA)	AAV9	Intravenous infusion
Hemgenix	2022	Certain kinds of Hemophilia B contains codon-optimised cDNA of the human coagulation Factor IX	AAV5	Intravenous infusion
Elevidys	2023	Duchenne muscular dystrophy Treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene	AAVrh74	Intravenous infusion
Roctavian	2023	Hemophilia A (factor VIII deficiency)	AAV5	One-time, single-dose intravenous infusion

### *The Challenges*

There are many challenges to overcome with regards to safety, efficacy, payload size, sustainability, and scalability when leveraging AAV for diseases linked to mutations in genes. From both a safety and efficacy perspective, the human immune system recognizes and responds to AAV vectors, potentially reducing the efficacy of the therapy or causing adverse reactions. Furthermore, patients with pre-existing immunity to AAVs from natural infections may have limited therapeutic benefit and may face safety risks.<sup>{3}</sup>

The manufacturing scalability of AAV vectors also poses a challenge to the growing demand for these viral vectors in various clinical applications.<sup>{4}</sup>

### *Tackling the Limitations*

Researchers are assessing different strategies to address these challenges. In one example, a study found that co-administering synthetic vaccine particles encapsulating rapamycin (SVP[Rapa]) with AAV vectors had the potential to modulate vector immunogenicity and allow re-administration.<sup>{5}</sup> Another study into the use of tolerogenic nanoparticles with hepatotropic AAV vectors suggests the potential for vector re-dosing by suppressing adaptive immune responses.<sup>{6}</sup>

More efforts will focus on modifying the AAV capsid through molecular engineering to reduce immunogenicity, implementing short-term immunosuppression during the administration of AAV-based therapies to reduce immune responses against the vector and developing new AAV serotypes with lower immunogenicity or that can evade pre-existing immunity.{7}

### **Lipid Nanoparticle (LNP) Delivery for mRNA and RNA**

LNP has proven to be a reliable drug delivery system for mRNA, particularly mRNA SARS-CoV-2 vaccines. In light of the success of these vaccines, there is growing momentum to develop LNP-based RNA therapeutics for various genetic diseases and cancers.{8}

#### *The Challenges*

Toxicity and unwanted immunogenicity remain concerns with LNP delivery at the higher amounts and systemic delivery that would be required for therapeutics. Even with vaccines which were administered in relatively low amounts intramuscularly, a minority of recipients experienced significant side effects.{9} In one example, researchers point to a pro-inflammatory role for ionizable cationic lipids, with intranasal administration of LNPs into mice leading to massive lung inflammation and high mortality.{10}

#### *Tackling the Limitations*

One approach that seeks to address toxicity concerns is targeted *in vivo* synthetic particle technology based on ionizable LNPs. Combined with transient gene editing, this technology promises to be potentially safer due to increased biodegradability and lower immunogenicity. It is also more scalable in terms of dose regimen and could potentially address a broader range of disorders.{11}

### **CAR-T Cell Therapies**

CAR-T cell therapies have been used to successfully treat hematological cancer.{12} There is widespread research into the use of CAR-T cells to treat solid tumors as well as to treat various other conditions such as autoimmunity, chronic infections, cardiac fibrosis, and senescence-associated disease.{13}

## *The Challenges*

Hopes for CAR-T to tackle solid cancers have been set back by a number of challenges, including severe toxicities, target heterogeneity, and limited tumor infiltration. Further, there are functional barriers, since CAR-T cells require expertise to create and administer, and engineering issues to scale out manufacturing so that the therapies are accessible to more patients. {14}

## *Tackling the Limitations*

Different pathways and approaches are being investigated to improve CAR-T therapies. One approach that aims to tackle loss of the antigen is to combine CAR-T cell therapy with specific vaccines to boost and maintain an effective CAR-T cell population. {15} Another exciting development is the use of *in vivo* induced CAR-T cells loaded with CAR-genes and gene-editing tools to tackle toxicity issues. {16} There is also growing interest in other T cell therapies, including gamma-delta T cells, invariant natural killer T cells, natural killer, and dendritic cells. {17}

## **Gene Editing**

One of the most exciting and rapidly developing fields is gene editing. In November 2023, the United Kingdom became the first country to approve Vertex's revolutionary gene editing, CRISPR-based treatment for sickle-cell disease and transfusion-dependent beta thalassaemia. {18} An FDA advisory committee meeting was held in October to discuss the product, known as exa-cel. Remarkably, the meeting did not question efficacy, but sought insight on off-target genome edits and potential additional studies to assess the risk of off-target editing.

## *The Challenges*

The greatest challenges facing gene editing are identifying the most suitable delivery systems and specificity. With *ex vivo* gene editing, while there have been important breakthroughs, such as exa-cel, *in vivo* approaches are required for targeting internal organs, such as the lung or heart.

## *Tackling the Limitations*

Current gene editing successes build on hematopoietic stem cell therapy, which is now standard treatment for leukemia. The clinics, quality standards, and understanding of how to treat patients are in place. While questions remain about gene editing, experts and regulators recognize the importance of the field. Already there are guidelines from FDA to support gene editing products and experts are excited about the potential of these products. As Dr. Scot Wolfe, a member of the FDA advisory committee panel assessing exa-cel noted: “We don’t want to let perfect be the enemy of the good. At some point we have to try things out in patients.”

## **Realizing the Promise of Gene Therapy**

Cell and gene therapy is proving to be transformative for patients with high unmet needs. While there are many challenges to overcome across all platforms, researchers are gaining a greater understanding of the obstacles faced—whether in development or treatment—and with that knowledge, new potential solutions are emerging.

*The contents of this article are solely the opinion of the author and do not represent the opinions of PharmaLex GmbH or its parent Cencora Inc. PharmaLex and Cencora strongly encourage readers to review the references provided with this article and all available information related to the topics mentioned herein and to rely on their own experience and expertise in making decisions related thereto.*

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**Dr. Jörg Schneider** is a Principal Consultant at Biopharma Excellence, a PharmaLex company, where he focuses on ATMPs/CGT products and is involved in regulatory interactions, nonclinical development, and strategic support for multiple clients. A translational biopharmaceutical expert, he has broad knowledge of different technologies and product classes such as recombinant viral vectors, cell therapies, oncolytic viruses, glycoconjugate vaccines, monoclonal antibodies, and non-antibody scaffold drugs.

## Psychedelic Therapy Saved My Husband's Life. How Can We Save More?

Angela Terhune-Hargrove, MHA



Open a newspaper. Scroll through social media. Watch the news. It's no secret that psychedelic therapy is on the verge of becoming the next big thing. In fact, this therapeutic area's growth is perhaps the greatest advancement mental healthcare has seen in a long time. But I might be a bit biased.

### Now I'm a Believer

I currently serve as Senior Director of Business Development and psychedelic subject matter expert at Elligo Health Research<sup>®</sup>. I've worked in addiction, clinical research, and in the mental health field for nearly three decades, but my deep commitment to advancing psychedelic therapy comes from a personal, harrowing ordeal.

My loving husband, a talented lawyer who runs a thriving business, grappled with profound mental health and addiction issues. Under immense professional pressure, a well-intentioned prescription for attention-deficit/hyperactivity disorder led my devoted husband down the treacherous path of Adderall addiction. This soon became the catalyst for his descent into abuse of alcohol and other substances. Our family was ensnared in a tornado of addiction and our household, once brimming with love and laughter, became a stage for traumatic events, hospitalizations, and a seemingly endless spiral of despair. With my mental health connections, I approached top-tier psychiatrists for help, but they inadvertently transformed my spirited husband into someone I no longer recognized: a zombie.

Amidst the chaos, he recalled his introduction to Dr. Deborah Mash's groundbreaking work with [ibogaine](#). Having grown up during the Reagan administration's War on Drugs, we had our reservations about psychedelic drugs. But what other options did we have? We found our way to the Avante Ibogaine Institute in the Bahamas, where under the astute care of an experienced and dedicated team, my husband underwent ibogaine therapy.

The transformation was immediate and astounding. I knew it worked the moment we were reunited because that twinkle in his eye, the spark I love so much, was back. With a renewed vigor for physical and mental health, he's now thriving as a loving husband, wonderful dad, and recovering addict who's been substance-free for six years and counting. He was only treated with ibogaine once.

### **How Many Others Can We Save?**

My personal experience with psychedelics aside, research has shown its incredible ability to relieve symptoms of anxiety, depression, post-traumatic stress disorder (PTSD), substance use disorder, and other mental health conditions. {1} In a survey of opioid-addicted patients who had undergone treatment with ibogaine, 80% reported that the psychedelic "eliminated or drastically reduced withdrawal symptoms," and 30% described complete opioid abstinence following treatment. {2} The nonprofit Multidisciplinary Association for Psychedelic Studies (MAPS) has also produced impressive results from its two MDMA (3,4-Methylenedioxymethamphetamine, or "ecstasy") therapy clinical trials for adults with PTSD, reporting that patients treated with MDMA treatment displayed "significant improvement over therapy with placebo when measured at two months after the last experimental session." {3}

But psychedelic therapy is at a crossroads. It could be the transformative tool we need to help patients for whom existing treatments are not enough. However, if we take only a few steps down the wrong path, it could also become yet another almost-breakthrough. What can we do to ensure psychedelic therapy's future?

### 3 Critical Actions to Secure the Future of Psychedelic Therapy

Based on my professional and personal experience, I suggest focusing on three key areas: education, safety, and specialty research sites.

#### *Education and Training*

Federal laws and policies, such as Nixon’s Controlled Substances Act and Nancy Reagan’s “Just Say No” anti-drug campaign, have negatively impacted the public perception of psychedelic therapy. {4,5} To negate negative perception and cultivate a more open-minded atmosphere in which these therapies can thrive, we must educate the public and the healthcare industry about the promising advantages and safety of psychedelic therapy. As history has demonstrated, we can rise above societal resistance. Medical innovations that were once met with apprehension and disbelief, such as organ transplantation, *in vitro* fertilization, and even vaccines, are now integral parts of our established standard of care.

#### *Safety Standards*

As with any other medical advancement, psychedelic therapy will only be fully accepted once it has rigorous safety and quality standards. The best place to start is by implementing such standards in psychedelic research. In June of 2023, the U.S. Food and Drug Administration released a draft guidance on psychedelic research, taking a big step in the right direction. {6} The guidance offers foundational recommendations to ensure subject safety and data quality, such as onsite psychotherapists to help patients make sense of their psychedelic experience and integrate what they learned into their lives. It also recommends a dual-monitor system to guarantee support and oversight throughout the treatment session, as well as more comprehensive disclosures to help patients understand that they might experience intense perception, cognition, and judgement changes during the treatment.

#### *Specialty Research Sites*

Many people who participate in a psychedelic clinical trial have never used psychedelic drugs or are suffering from intense symptoms that put them in a precarious state of mind. Therefore,

given the novel and potentially overwhelming nature of psychedelics, it's essential that research sites offer a calm, comforting environment in which the trial participants will feel safe and comfortable. Details such as covering mirrors, offering private restrooms during the treatment, and cultivating a serene and welcoming waiting room can be integral to the patient's experience and the study's success. Any sponsor or site undertaking psychedelic research must be prepared for and enthusiastic about the extra time, effort, and resources it will take to help the therapy reach its full potential, making specialty sites even more valuable to psychedelic advancement.

### **The Time is Now**

The profound transformation in my husband's life is a living testimony of the healing power of psychedelics at a time when so many Americans are desperate for answers to their suffering. If we promote education, ensure patient safety, and cultivate specialty sites, imagine how many more lives we can save.

As both a mental healthcare professional and the wife of a man who is alive and thriving because of these groundbreaking therapies, I am ready to put in the work to secure psychedelic therapy's future. Are you?

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**Angela Terhune-Hargrove, MHA,** ([angela.hargrove@elligodirect.com](mailto:angela.hargrove@elligodirect.com)) is an accomplished Senior Business Development and Clinical Research Professional within the pharmaceutical/contract research organization, psychedelic research, central nervous system, biotech, over-the-counter, cannabis, and dietary supplements industries who is known for fostering and leading teams that transform patient care and optimize operations.

BY THE NUMBERS

## From Big to Little: Numbers that Matter in Today's Clinical Research Enterprise

Curated by Gary W. Cramer, Managing Editor for ACRP



**\$34 billion** The approximate amount of revenue generated by the top 10 contract research organizations in 2022, representing an estimated 69% of total revenue spent on contract clinical services globally.

Source:

<https://www.appliedclinicaltrials.com/view/outsourcing-model-usage-and-its-relationship-to-clinical-trial-performance>

**\$2.2 million** The per-patient cost of treatment with a newly U.S. Food and Drug Administration–approved, CRISPR-based therapy for sickle cell disease, the first to use the gene-editing tool.

Source: <https://www.nbcnews.com/health/health-news/fda-approves-cure-sickle-cell-disease-first-treatment-use-gene-editing-rcna127979>

**20,109** The number of drugs in the research and development pipeline in 2022, up from 17,737 in 2020.

Source: [https://www.contractpharma.com/issues/2023-06-01/view\\_features/cro-industry-report/?widget=listSection](https://www.contractpharma.com/issues/2023-06-01/view_features/cro-industry-report/?widget=listSection)

**6.79 vs. 0** The number of cancer clinical trials per 10,000 individuals run from 2005 to 2023 in the province of New Brunswick, Canada, as opposed to the number run in Canada's three territories.

Source: <https://medicalxpress.com/news/2023-12-reveals-inequities-access-cancer-clinical.html>

**2% to 14%** The rate at which all adolescents and young adults are estimated to participate in clinical trials.

Source: <https://breakingcancernews.com/2023/11/28/ayas-in-clinical-trials-underrepresented-and-underserved/>







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