Clinical Researcher™

The Authority in Ethical, Responsible Clinical Research

November 2019 (Volume 33, Issue 9)

Charting Early and Changing Career Courses

Clinical Researcher™

Clinical Researcher—November 2019 (Volume 33, Issue 9)

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EXECUTIVE DIRECTOR'S MESSAGE

Straightening Out Those Sideways Career Entries

Jim Kremidas

I recently had the opportunity to watch some fascinating—and inspiring—interviews with members of ACRP's Northern California chapter. Enthusiastic participants talked about the importance of clinical research to them as a career, both personally and professionally. Over and over, I heard uplifting stories of how a clinical trial professional had seen his or her work improve the lives of patients and otherwise offer new hope in the face of sometimes desperate health circumstances.

I was struck by another theme that recurred during the dozen or so interviews: How virtually none of the clinical research coordinators (CRCs) in the group had *set out* to become clinical researchers. Many "entered the field sideways," as one put it, via another aspect of healthcare, such as nursing. They described how roundabout entry points, fortuitous connections, and maybe a little luck had brought them to such a fulfilling professional landing place.

Frankly, I was left with mixed emotions. On the one hand, I remain so grateful our field was able to somehow attract and retain these hard-working, motivated professionals. On the other hand, I had to wonder about how much talent we may be missing because clinical trials lack clear entry portals and career paths.

Progress on Pathways, Partnerships, and Professionalism

Working with you, our members, and others throughout the clinical trial ecosystem, ACRP has made some exciting strides when it comes to helping establish meaningful, role-specific competency guidelines, performance-based milestones, and career paths. All are designed to help us address a chronic workforce shortage by enriching the talent pool and helping the best of the best remain vibrant performers throughout the cycle of their careers.

The good news keeps coming. Earlier this month, we welcomed OhioHealth Research Institute to the ACRP "Partners in Workforce Advancement" (PWA) project, our groundbreaking new initiative to expand the clinical research workforce by bringing together a broad coalition of clinical research stakeholders focused on creating a sustainable workforce for the future.

We are excited to partner with OhioHealth Research Institute on this critical initiative. We believe that in clinical research, people are everything. Without an adequate pipeline of qualified, competent professionals, our community will fail both to sustain the workforce and to improve the efficiency and quality of medical discovery.

I look forward to working more closely with each of you in 2020 on these and other important issues. As always, please feel free to reach out to me directly with your ideas and concerns.

Jim Kremidas (jkremidas@acrpnet.org) is Executive Director of ACRP.

PEER REVIEWED

Cystic Fibrosis Clinical Research Coordinator Mentoring Program: A Review

Zoe Davies, NP, MS, CCRC; Colleen Dunn, MS, RRT, CCRC; Elizabeth Hartigan, MPH, RN, CRM; Kathleen Hilliard, CCRC; Patricia Burks, RN, MA, CCRC

Cystic fibrosis (CF) is an inherited, autosomal recessive, multisystem disease that affects approximately 30,000 individuals in the United States{1} and is caused by mutations in the gene that produces the CF transmembrane conductance regulator (CFTR) protein. CFTR is chiefly responsible for the transport of ions and fluid across epithelial cell membranes, such as those found in the lung, pancreas, liver, gastrointestinal tract, and skin. The abnormalities in the lung lead to airway obstruction, inflammation, and infection, which cause progressive airway damage and account for most of the morbidity and mortality seen in CF.{2}

Huge advances have been made in recent years in the knowledge about the defective gene that causes CF, its defective protein product, and the downstream clinical consequences for people with CF. This, in turn, has led to the development of multiple therapies which have improved the mean life expectancy for a person with CF to approximately 44 years of age.{1} These advances are the result of successful clinical research efforts supported, in part, by the Cystic Fibrosis Foundation (CFF).{3}

In collaboration with industry and academic partners, the CFF has developed a robust drug development pipeline to meet the overall mission of improving the lives of patients with CF. Key limiting factors to moving multiple therapies forward simultaneously have included both recruitment of subjects (since CF is considered an "orphan disease" that affects less than 200,000 people nationwide) and the availability of trained clinical research staff.{3} Recognizing this need, the CFF founded the CF Therapeutics Development Network (TDN) in 1998.{3}

The CF TDN was initially comprised of eight clinical research centers, but over the years it has expanded to its present total of 92 centers.{4} The development and expansion of the CF TDN has helped to ensure broad geographic distribution of CF clinical research centers across the United States, thereby increasing access for many additional eligible CF patients. As these new centers have been added to the network, a key goal has been to ensure that each one has dedicated, well-trained CF researchers—particularly clinical research coordinators (CRCs)—available to conduct the research.

Additionally, CRC turnover and retention are important issues facing most research programs, regardless of clinical indication. According to a 2017 survey conducted by SCORR Marketing,{5} 41% of research professionals are considering switching jobs and don't see much opportunity for career advancement within their organizations. Prior to 2008, CRC turnover in the CF TDN was *believed* to be due to the length and complexity of many of the CF research protocols, which often require specialized training; the long, often tedious working hours; the lack of career advancement; and less than optimal pay. To a new CRC, these issues can be overwhelming.

Recognizing the crucial role of the CRC, the CFF decided to pilot a CF CRC mentoring program modeled after a similar program developed for CF dieticians. The main goals of this program were to provide resources, training, and networking opportunities to those new to the CF research world, with the hope of increased retention of those same CRCs over time.

Program Description{6}

In 2008, this program consisted of four keys roles (see Figure 1):

Team Leader—This person provided oversight for the entire mentoring program. The team leader coordinated all activities related to the program and served as a conduit between the CFF and the TDN. This person also helped to develop the materials needed for the program and facilitated conference calls, site visits, and e-mail contacts.

CF CRC Facilitator—The facilitators served as the organizational conduit between the mentors and the apprentices. They helped to develop and oversee the mentoring curriculum and made sure that the mentors and apprentices were "a good fit" for each other. Interactions included face-to-face meetings, site visits, phone, and e-mail contacts.

CF CRC Mentor—Served as a resource for new CF RC apprentices. The interactions included a face-to-face meeting, a site visit from the apprentice to the mentor's site, phone, and e-mail contacts for at least three months after the site visit.

CF CRC Apprentice—Individuals who were new to CF research and who intended to continue in CF research after program completion.

Figure 1: Key Roles of the CF CRC Mentoring Program
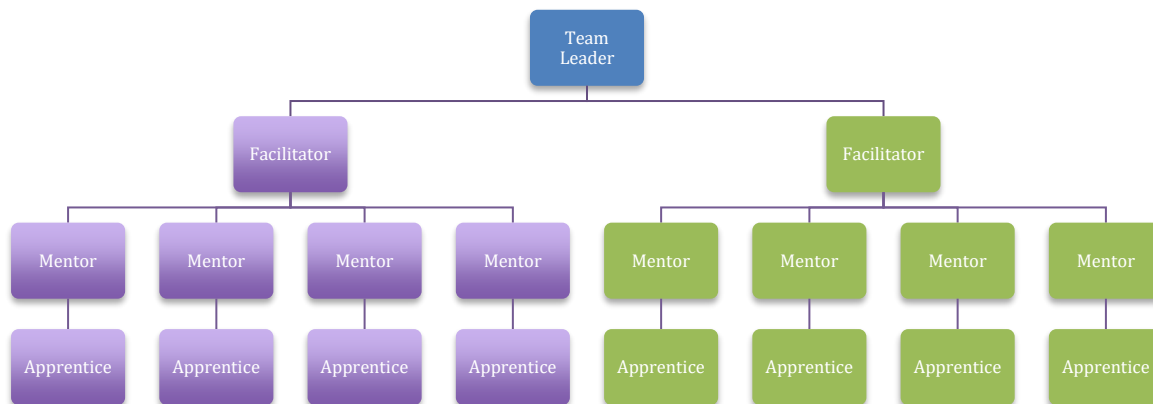
Today, the organizational structure remains much the same with one exception: The two facilitators absorbed the team leader position/responsibilities in 2013.

History

The rollout of the program was initially announced at a national CF CRC retreat as well as advertised on the CF CRC TDN website. Individuals for the first group of mentors were handpicked by the CF mentoring program executive committee (the team leader, facilitators, and a representative from the CFF and TDN), and those interested in being an apprentice were required to fill out an online application. The team leader and facilitators matched the available mentors to apprentices depending on various criteria; for example, patient population (adult, pediatric, or both), the specific type of experience needed, and geographical location.

The facilitators then contacted the mentor/apprentice pairs to notify them of the match as well as help to "facilitate" the overall mentoring experience. Each mentor contacted his or her apprentice to determine the specific learning needs, help develop goals and objectives, and set up a date for the site visit. Once the site visit was over, the mentor and apprentice as well as the apprentices' principal investigators (PIs) were required to complete an evaluation of the process. The mentor was also required to maintain contact for three months following the visit to provide additional support as needed.

After the apparent success of the first group of CRC apprentices in 2008, it became a regularly scheduled program offered to new CRCs within the TDN network once or twice per year. As each cohort of mentors and apprentices completed the program, any issues that had occurred during that particular match period and the post-visit evaluations were reviewed and discussed by the program leadership. This provided important feedback, which was used to update and improve the overall program; for example:

- A web-based application process using Survey Monkey is now the method that both apprentices and mentors use to apply to the mentoring program, as well as for completion of the post-visit evaluations.
- Application questions were streamlined and/or rewritten to better identify "best" candidates.

- Post-visit evaluation questions were modified in order to better understand the individual's experience.
- PI awareness and engagement is crucial for the success of the program; now they are involved from the beginning of the application process through program completion.
- To fine-tune presentation and lecturing skills, apprentices are required to present their goals and objectives, as well as a mid-and post-visit summary, to the group.
- Program documents, power point presentations reviewed and updated on a yearly basis.
- Added specialty mentoring tracts (i.e., program management, regulatory, and laboratory).

In Retrospect

After 10 years of program implementation, a retrospective review was completed to ascertain if the program was indeed providing the necessary support, resources, and training to participants. All of the post-visit evaluations obtained from the apprentices, mentors, and PIs from 2008 until 2018 were sorted and reviewed. As edited for clarity and listed below, the questions required either open-ended, best answer, or yes/no responses (see Figures 2, 3, and 4 for highlights from the responses).

<u>Apprentice</u>

1) The CF CRC mentoring program met my expectations.
2) The CF research program has improved at my center since I participated in the mentoring program.
3) I feel I am more knowledgeable and active in CF research since I participated in the mentoring program.
4) Please briefly describe the site visit, explain what the focus of the visit was, and provide examples of what you took away from the visit.
5) Do you feel that you were adequately prepared for the visit?
6) After the site visit, please list any processes/changes you would like to incorporate at your center to improve site performance.

7) After consultation with your mentor regarding clinical trial and site management processes at your site, describe the focus of your interactions with your mentor or your learning plan.

8) Name a tool from the CF ClinicalResearchNet Toolkit (see * below) that you were able to implement at your center.

9) What do you consider the most positive change you have made in your research program as a result of the CRC mentoring program? (see ** below)

Figure 2: Apprentice Responses from Review (%)
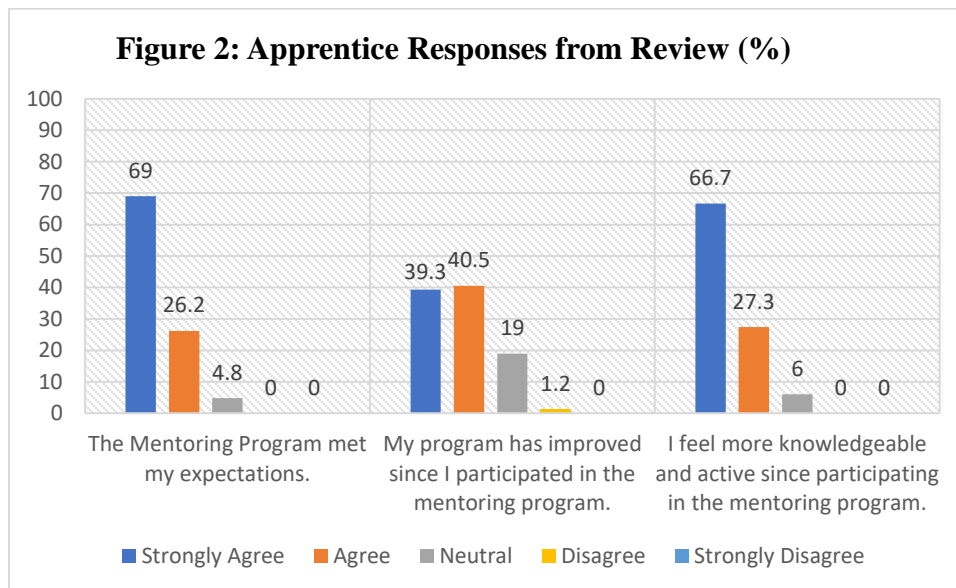
*The toolkit contains numerous "tools" specifically for the CF CRC. The most commonly implemented tool(s) included the templates and checklists for facilitating study startup and the site budget tool to help create appropriate study budgets.

**Participating in the program helped apprentices better identify areas for improvement at their own sites, improved their overall communication skills, and facilitated networking with their colleagues.

Mentor

1) The CF CRC mentoring program met my expectations.

2) Were interactions with the facilitators helpful?

3) Please briefly describe the site visit and what the focus of the visit was**.**

4) Do you feel that you were adequately prepared for the visit?

5) After the site visit, list three things that you think would improve performance at the apprentice's site.

6) After consultation with the apprentice regarding clinical trial and site management processes at their site, describe the focus of your interactions or your learning plan.

7) Name a tool from the CF ClinicalResearchNet Toolkit that your apprentice was able to implement at his/her center.

8) I think the CRC mentoring program makes a difference in the CRC community at large.

Figure 3: Mentor Responses from Review (%)
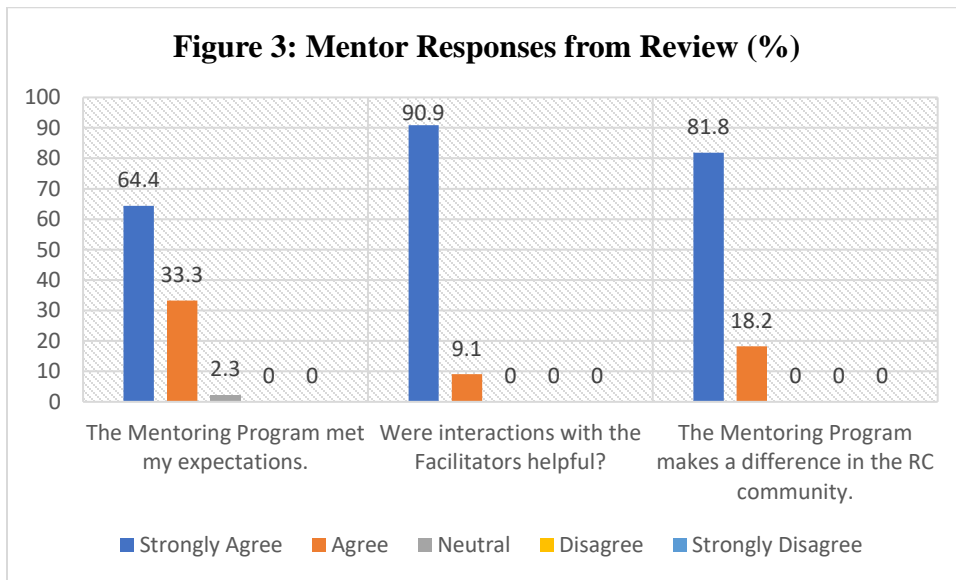
PI

1) The CF CRC mentoring program met the expectations of the CRC at our site.

2) The site visit provided our CRC with more knowledge in CF research.

3) Have you and your CRC identified a process that you intend to evaluate and improve?

4) Have you and your CRC been able to make a plan to address improvement changes?

5) List the new tools your site CRC has been able to implement at your center.

6) List changes noted in your research program since the CRC at your site participated in the mentoring program.

7) Was there an impact on the partnering between the PI, clinic nurse/coordinator, and CRC at your site after your CRC participated in the mentoring program?

8) Fostering leadership skills was an inherent part of the mentoring program. Have you witnessed an enhancement in this since your CRC participated in the program?

9) What project(s) is your CRC planning to work on over the next year?

Figure 4: PI Responses from Review (%)
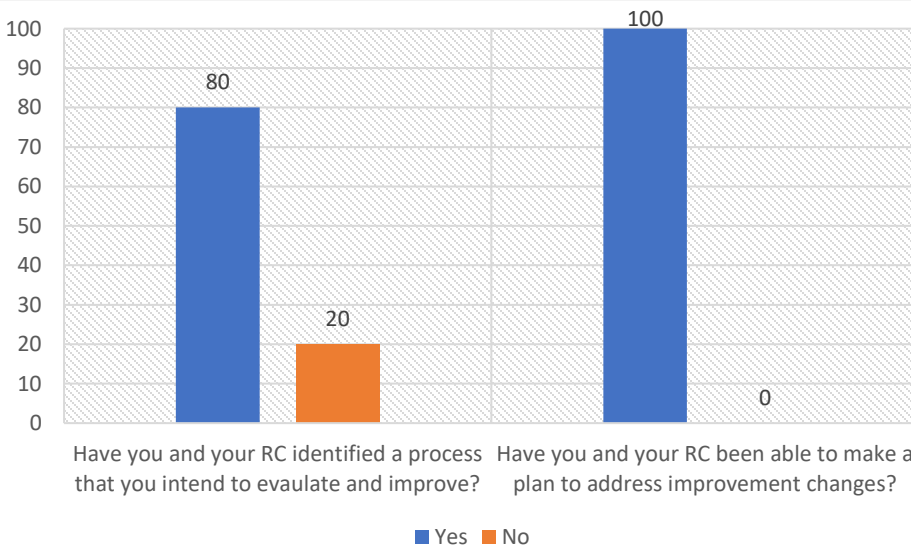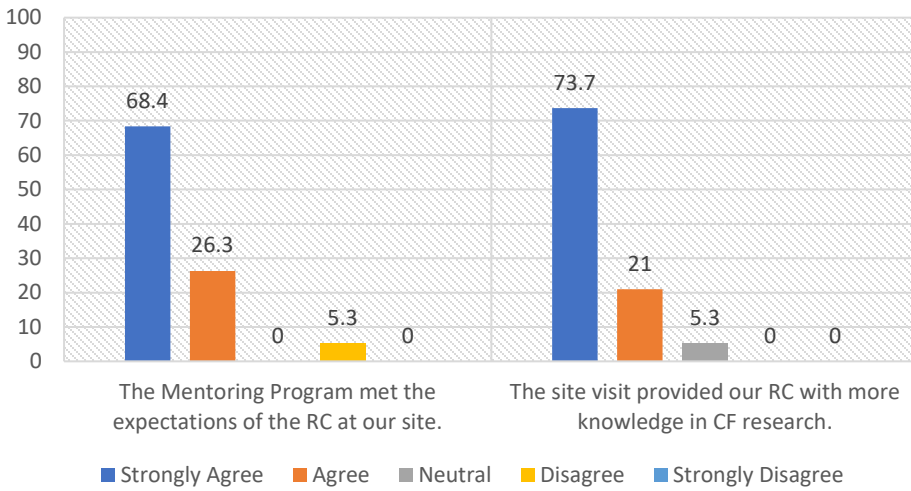
Apprentice Comments

"Thank you so much for the opportunity to participate in the [mentoring program]. As a coordinator new to research entirely and the only CF research person at my site, this program has showed me how supportive and helpful the CFF/TDN community is and their commitment to fostering growth as coordinators."

"I am so thankful for being given this opportunity by the TDN. I will forever be grateful for the people I met in this program and for everything I've learned that I will take with me throughout my career."

"I had a wonderful experience and am grateful for the opportunity. My mentor is very knowledgeable and admirable. I'm certain this program contributed to improved performance of research for me, individually, and for our center."

Mentor Comments

"I love this program and the opportunity to network with new coordinators. They give me energy and new ideas. Thank you for the opportunity."

"What a wonderful program. We were able to connect at NACFC and sit in sessions together. We have continued our mentor relationship, talking briefly at least [monthly], sharing concerns [and] milestones, and having opportunity for learning from each other."

PI Comments

"I felt the program to be extremely valuable. I hope the [mentoring] will continue in the future."

"Nancy, our new [coordinator], has taken huge initiative to move our CF research program forward. We couldn't do it without her."

"My [coordinator's] mentor spent the day with her then disappeared to who knows where. Thus [she] never received any of the helpful handouts, spreadsheet formats, etc. that the mentor had promised her. Disappointing."

Status Update

By the end of 2018, 102 apprentices had completed the program: 53 (52%) of those individuals are still working as CF CRCs and 49 (48%) have since left the position. Eight (7.8%) of those apprentices eventually became mentors. There were 50 mentors, 35 (70%) of which are still in CF research and 15 (30%) of which have since left the position.

Conclusion

The data show that the vast majority of participants feel that the mentoring program is indeed a worthwhile endeavor providing new CF CRCs with tools, ideas, and support for increasing their CF knowledge base and helping make their jobs more manageable. CRC turnover continues to be an issue, but once a CRC becomes a mentor, he or she seems more likely to remain in CF research.

In September 2016, in order to track turnover rates and determine the common reasons for leaving, the TDN decided to initiate CRC exit interviews. At the time of article submission, there were 71 completed interviews. CRCs indicated issues with coworkers and supervisors, pay, and lack of career advancement as influencing their decisions to leave the job. Interestingly enough, the length and complexity of protocols and the long, often tedious working hours were not significant issues. Mentors left their positions mainly due to retirement or career change/advancement within their institutions.

Obviously, continuing to obtain post–apprentice visit surveys as well as completing CRC exit interviews will be important to help with mentoring program development, which in turn will hopefully help improve overall job satisfaction and retention amongst CF CRCs.

Acknowledgements

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Evaluating the Role of the Regulatory Writer

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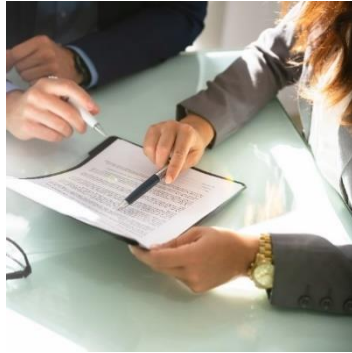
Drug development is a billion-dollar industry featuring a variety of roles necessary to pursue the goal of product approval.{1} A crucial component within this process is well-developed, well-documented, and well-communicated study research practices. Medical writers act as key communicators for study sponsors and governmental agencies, such as the U.S. Food and Drug Administration (FDA) and European Medicines Agency, to evaluate coherence, ethics, and efficacy of research practices and results for drugs and medical devices/diagnostics.{1–3}

Medical writers either within pharmaceutical companies or via contract research organizations (CROs) can be further divided by specific writing role and key composition types, such as *promotional* and/or *advertising, non-promotional education/training (*e.g., *medical affairs), publication, labeling,* and *regulatory writing,* as described in the following:

- Advertising and promotion utilize a unique set of regulations for postapproval communications to market the respective product to patients and/or healthcare providers; 21 CFR 202-203 in the FDA's *Code of Federal Regulations* and many guidance documents direct writers in this arena.
- Non-promotional education or training materials are often geared to professional audiences, such as key opinion leaders or medical affairs professionals, respectively.
- Publication writing summarizes clinical research procedures, analysis, and results into journal manuscript formats or conference materials, such as presentations, abstracts, and posters.

- Key examples of labeling documents include therapeutic ingredients, dosing directions, and warnings on the exterior of therapeutic packaging and inserts; the core purpose is to update and list all risks and directions for safety of therapeutic use following approval.
- Regulatory writing is the development of preclinical and clinical research procedures into documents and submission packets that review and record essential study conduct, practices, and results.{2,3} Writers within this discipline ensure clarity of study statistical analyses, protocol guidelines, toxicology reporting, and completion of study and governmental agency-specific documentation and submission packets needed for approval and ongoing research practices.{2,3}

In summary, Table 1 reviews the key types of medical writing and provides brief descriptions and examples of content.

Table 1: Key Types of Medical Writing

Medical Writing Types	Brief Description	Examples of Documents
Promotional/advertising	Composition of therapeutic and product information to patients/consumers and clinicians for commercial and instructional use	Promotional presentations, direct-to-consumer ads, sales aids (e.g., brochures), and digital/media promotion (e.g., websites, social media)
Non-promotional education/training	Composition of therapeutic and product information to educate clinicians and other medical professionals	Internal educational/ training content (e.g., advisory board slide decks) or external scientific content (e.g., exposition information, standard response letters)
Publication	Composition of study design/methods, data analyses, and clinical trial results of an intervention(s) or studied medical topic for peer review	Journal manuscripts; conference materials such as posters, abstracts, and oral presentations; and internal documents (i.e., publication planning)
Labeling	Composition of medical directions and warnings	Drug labels, package inserts/instruction pamphlets, warning

		for drug use to patients and clinicians	boxes/lists, lists of active/non-active ingredients
	Regulatory	Composition of study documents for use in research conduct and summary of research results	Informed consent form, study protocol, clinical study report, risk evaluation and mitigation plans

The regulatory writer is the focus of this review, and this role can be represented by a variety of individuals from multiple backgrounds, experiences, and education.{1} However, there is a lack of published literature of the necessary proficiencies and specific tasks required of regulatory writers.

A forum held by the American Medical Writer's Association (AMWA) in 2019 reported the need for, and difficulties associated with, organizational efforts to recruit and train medical writers in the regulatory field.{4} This paper explores and characterizes the attributes and importance of the regulatory writer role in drug development as it may pertain to small-scale pharmaceutical or biotech companies. Moreover, defining the practices and requirements of a regulatory writer can encourage interest in, and inspire novice candidates to consider joining, this field.

Select Examples of Regulatory Documents for Regulatory Writers

Regulatory writing includes a variety of documents utilized in different functions in the conduct of clinical research. The following sections summarize several core research documents that are chiefly written by regulatory writers.

Informed Consent Form

Informed consent forms (ICFs) are the main documents used by study site personnel for familiarizing potential volunteer subjects with the details of a specific clinical trial. Per international and governmental agency criteria, such as FDA's 21 CFR 50, volunteers cannot proceed into the study protocol activities without first providing voluntary consent via the ICF, after having a discussion about any and all risks associated with study interventions, as well as

about the participant requirements for completing the study. ICFs should include information on any possible adverse events and on the study's purpose/practices, so regulatory writers must have insight and knowledge of the study protocol to ensure all the study parameters are summarized.

From a participant perspective, appropriate "understanding" of an ICF is imperative to adequately *inform* the participant of risks. There are different levels of understanding, including objective vs. subjective understanding (i.e., correct knowledge vs. personal impression of facts) and general understandability—all of which need to be considered in ICF creation.{5} Further, a study comparing ICFs over a period of 17 years for rheumatology studies identified a need for ICFs to be written between a third- and eighth-grade reading level.{6}

Conciseness is another important component in ICF creation, whereby higher page counts in ICFs result in participants being less likely to fully review document content.{6} Developing and abiding to structural ICF templates can assist regulatory writers so that content is full and clear.{7} Additionally, regulatory writers need to reliably incorporate multi-disciplinary feedback (e.g., from legal experts and clinicians) all while ensuring the participant will fully understand the document.

Study Protocol

Regulatory writers help to develop the protocol's explanations of guidelines and study procedures with oversight and input from the study investigators.{2,3} Protocols usually follow a generalized structure that includes sections on therapeutic background, study design, inclusion and exclusion criteria for participation, treatment formulation and administration criteria, toxicities and reporting criteria, statistical considerations for efficacy determination, and appendices to summarize section content in figure and tabular form (21 CFR 312).

Regulatory writers also assist with the memos and amendments to the study protocol to establish additional information and altered directions for therapeutic use and minimization of risks. Regulatory writers must ensure these modifications are articulated coherently and be responsible for version control across affected documents (e.g., protocol sections and study supplemental materials)—all in a timely fashion.

Clinical Study Reports{8}

Clinical study reports (CSRs) act as comprehensive summaries of the efficacy, accumulated toxicity, and other statistical outcomes of clinical data, and are one of the International Council for Harmonization (ICH) E6 Essential Documents following a clinical trial. Regulatory writers are tasked with composing these reports about the safety and efficacy raw data outputs, which can be quite extensive with a multitude of statistical variation.

Per FDA guidance and ICH E3 criteria, CSRs should specifically include participant demographics, review of each proposed outcome, and review of adverse events that have occurred. Regulatory writers require a strong understanding of guidance documents/guidelines for characterizations and completeness over the outcomes of statistical analyses and tabular and/or graphical constructs.

Risk Evaluation and Mitigation Strategies{9}

Risk evaluation and mitigation strategies (REMS) are developed as guides to educate consumers about warnings/safety issues concerning a drug and to give specific directions for therapeutic use. REMS plans have become a requirement for certain pharmaceutical products since initiated by the FDA Amendments Act of 2007 in order to impose greater safety measures on those therapeutics with seemingly higher risk-to-benefit levels. Regulatory writers document step-by-step instructions and/or safety precautions for patient use that would also be included within the New Drug Application (NDA) submission review to FDA.

Additional FDA Submissions{10,11}

Governmental agency submissions for clinical trial initiation or drug marketing require completion of specific forms and attenuation of several different study documents within the submissions. Regulatory writers often develop these large submissions, such as for Investigational New Drugs or NDAs, assembling investigator summaries, protocols, CSRs, integrated summaries of safety, and other sources of information. Amendments to any of these documents require complete updating and re-submission of the documents with a brief summary of the submitted changes.

Core Expertise of a Regulatory Writer

Inherent Proficiencies

In order to identify an individual's interest or suitability to the role of a regulatory writer, an implicit set of expertise must be demonstrated. The role requires collaboration with many members of the research team, such as the sponsor, research site investigators, statisticians, research managers, and/or coordinators. Regulatory writers in pharmaceutical companies or CROs often have direct communication among these team members by way of telephone, in-person contact, and/or e-mail to be able to obtain, verify, and deliver content for institutional review board, sponsor, and/or governmental agency review submission. Below are key proficiencies often not evident with merely a degree or certificate:

- Clear and accurate communication: Content must be written in a manner that is comprehensible to the entire research team. For example, protocols used to describe the intricacies of a clinical study should be written to allow for all researcher roles to properly understand each section. Clarity and concision are valuable characteristics, especially in composition of study documents for general audience (e.g., ICFs). Additionally, regulatory writers often interact with various disciplines, making professional and clear communication skills vital to this role.
- Agility and reliability: Timeliness is essential to ensure study conduct meets requirements for submission. In accordance with governmental specific regulatory documentation, regulatory writers must have awareness of submission details and deadlines. Regulatory writers need to respond to rapid changes in protocols and other documents that require fast updates, making adaptability and efficiency important skills. Additionally, deadlines are often immovable (e.g., following FDA approval or for NDA submission), elevating the need for project and time management skills.
- Data comprehension and dissemination: Volumes of raw data need to be dissected and accurately communicated in many types of regulatory documents. Regulatory writers are required to have a basic understanding of statistics and medical information in order to choose the most appropriate outputs that convey a true reflection of the trial (e.g., protocol, results in CSR).

- Document management: Lastly, regulatory writers are in charge of the collection, recording, and management/upkeep of various regulatory documents that are required by law per governmental agency for ethical review of drug marketing. These various documents require proper organization and time-sensitive submission per report type. Additionally, requests to update study details require all regulatory documents and components (sections, tables, figures, and supplemental materials) to be edited accordingly.

Academic and Real-World Experience

To be successful, regulatory writers harness various skills in order to provide detailed and appropriate regulatory document compositions by accessing their education, research experience, and knowledge of regulatory science.{2,3} The following summarizes key areas of expertise, with some overlap possible:

- Formal education: Regulatory writers must have a solid educational background to demonstrate adeptness for writing within the respective specialty. A master's degree and/or a connection to clinical research is desirable in order to obtain competencies of reviewing and interpreting statistical data results; moreover, the ability to simplify all research procedural communications to the variety of research roles is essential. In an assessment of regulatory job postings from 2009 to 2011, 68% of those analyzed required a scientific degree.{3} However, it should be noted that an advanced degree is not always required, and that work experience is a significant factor for success.
- Editorial and software competence: Regulatory writers should also be equipped with refined editorial skills, since they verify and edit a multitude of documentation to reduce likelihood of errors and ensure completeness. As noted earlier, superb communication skills are needed for computation and interacting with the research team regarding expectations and expert analyses of data such as within CSRs, safety reports, or amended documents.{2,3} Each company may also utilize its own software for data outputs or document containment; hence the regulatory writer should be familiar with and comfortable traversing many types of software. These skills can be learned through

literacy courses and/or onsite experience per preferences of the sponsor and/or governmental body.

- Real-world training: Direct research experience within the topics related to clinical research (e.g., oncology) is also highly valuable in order to more easily translate and utilize verbiage associated with the evaluations of therapeutic safety and efficacy results (e.g., pharmacovigilance, toxicity reports). This experience can also provide the regulatory writer with knowledge of the clinical research workflow and previous completion or orientation to respective documents. In addition to working experience within the clinical research field, continuing education courses on clinical research practices from organizations such as the Regulatory Affairs Professional Society (RAPS), Drug Information Association (DIA), and the Association of Clinical Research Professionals (ACRP) can be utilized. Networking among clinical research professionals and medical writers is another valuable experience that can help to increase awareness of, and connect a regulatory writer to, the aforementioned areas.

- Regulatory expertise: Regulatory writers require deep understanding of regulations governing research conduct, as well as of the respective governing bodies.{2,3} A thorough understanding of regulations and guidance documents is crucial for content development, along with governmental agency–specific expectations for reporting and submitting those documents. Knowledge of regulatory requirements can be demonstrated by previous work experience, education, and/or professional certifications such as Regulatory Affairs Certification (RAC) from RAPS. Experience in governmental regulatory policy, statistical methodology, biological mechanisms, therapeutic indication, and pharmacology are other desirable competencies for a regulatory writer.{2,3} Work experience in these areas allows for a more seamless transfer of data and an accurate data "storyline" in a wide variety of document types.

In summary, Figure 1 reviews key elements of a regulatory writer by role, responsibilities, and qualifications.

Figure 1: Key Elements of a Regulatory Writer
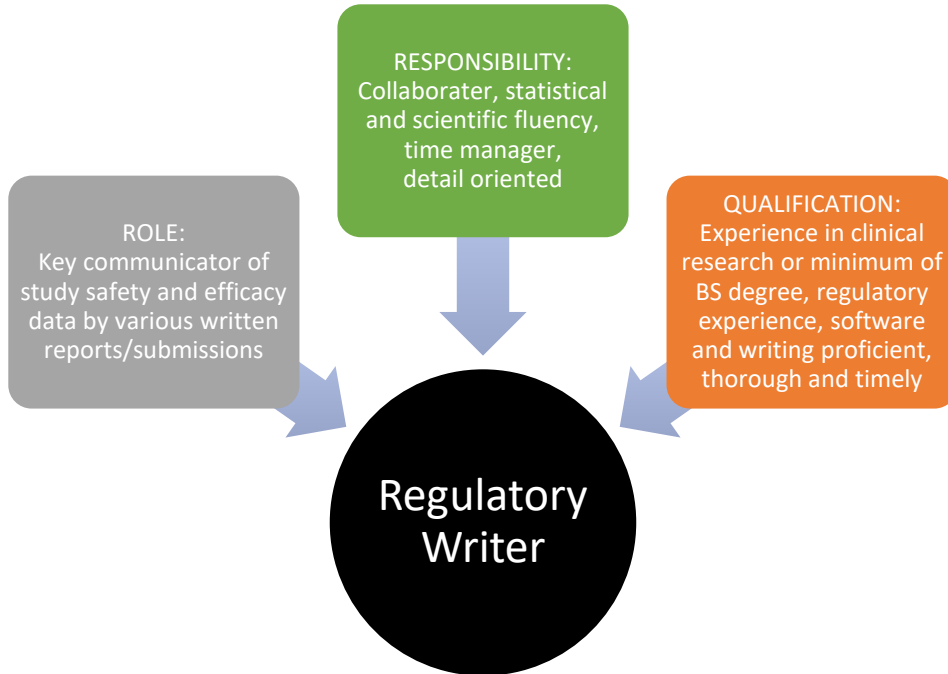
Conclusion

Regulatory writers have been identified as an important component of clinical research, and may act as the main communicator among the researcher roles and governing bodies concerning required research procedures and reports. An efficient regulatory writer demonstrates expertise in clarity and attention to detail, timeliness, and collaboration.

Pharmaceutical companies and CROs may approach the regulatory writer's responsibilities with a greater concentration on specialized regulatory writing assignments. In addition, lengthy research documents can be assigned to a group of regulatory writers rather than an individual, depending on submission timelines and individual workloads. As such, written communication is the crux of successful regulatory writers' output—within their team, to governmental bodies, to clinical study staff and investigators, and possibly to study participants/patients—with the ultimate goal of patient safety throughout a product's lifecycle.

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DATA-TECH CONNECT

Three Biopharmas Speed Trials by Modernizing Clinical Data Management

Henry Levy

Clinical teams are under enormous pressure to reduce cycle times and accelerate trials to completion. It costs an estimated $2.6 billion to get a drug to market{1}—twice as much now compared to 15 years ago. Study delays can contribute $800,000 to $8 million per day, highlighting the need to drive more efficient clinical trials.

At the same time, studies have become increasingly complex and the number of endpoints and procedures are growing, making data management timelines longer. Average times to build and release databases and lock study data have both increased over the last 15 years.{2}

Three biopharmaceutical and biotechnology organizations—Vertex Pharmaceuticals Inc., Lotus Clinical Research, and Cara Therapeutics—are reversing this trend. By adopting a modern electronic data capture (EDC) system and streamlining clinical data management processes, the companies have improved performance throughout the clinical trial lifecycle.

Vertex Pharmaceuticals: Shorter Build Times, Higher Operational Excellence

Operational excellence is a core principle at Vertex. Since 2017, the global biotechnology company has been outperforming industry averages for data entry and data lock cycle times; its EDC data are typically entered by sites within 48 hours and data locks are completed within 15 to 18 days. Only its database build times, averaging 12 to 14 weeks, were slower than desired.

The company set a goal to shorten build times to six to eight weeks, with completion to always come before the "first patient first visit" milestone. The data management team needed a modern, agile EDC that would support process changes to reduce build times, while maintaining the highest standards.

"You can't compress a 12 to 14–week timeline to six weeks by just working faster," said Vikas Gulati, executive director for clinical data management and metrics at Vertex. "Likewise, there is no benefit in shortening database build times if it impacts quality or extends lock times."

Traditionally, Vertex would author and provide its EDC vendor with a detailed specification document, commonly called "a spec," detailing study build requirements. To shift toward spec-less design, its current EDC vendor built a study template based on Vertex's standards library for electronic case report forms (eCRFs). With the study template, the vendor now works directly from the study protocols. This eliminated the process of authoring and reviewing a spec, saving Vertex weeks with each study. Adding cross-functional design reviews to the build process preserves the thought, rigor, and oversight that goes into ensuring the EDC is capturing the correct data and running the appropriate checks.

Reusing forms from a library or a template study greatly increased the efficiency and lowered the effort of building studies, especially for an organization like Vertex that focuses heavily in one therapeutic area. In the first two studies with its current EDC solution, only one net new form needed to be created. The rest were pulled and modified from the standards library.

Tied to the template study and the re-use of forms was the adoption of a risk-based approach to user acceptance testing (UAT) enabled by an EDC innovation called a differences report (see Figure 1). The differences report allows the data management team to see differences between two studies, including additions, omissions, or changes. Using the template study as reference, Vertex no longer performs UAT on the forms that were previously tested. The re-use of forms from the template study dramatically reduced the amount of testing needed.

Figure 1: Study Differences Report

Field	Difference	Template Study	Current Study
▬▬▬▬▬	Same	▬▬▬▬	▬▬▬▬
▬▬▬▬	Same	▬▬▬	▬▬▬▬
▬▬▬	Same	▬▬▬▬	▬▬▬▬
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Documenting any and all differences between two studies provides valuable documentation for UAT, go-lives, and protocol amendments.

For the forms that still needed to have UAT performed, Vertex abandoned the traditional "ping-pong" approach to UAT—a process of sending a casebook back and forth between the vendor and study team that could take up to two weeks per round. Instead, Vertex adopted a live, real-time UAT model in which the stakeholders of the study gather in a single room with the vendor to make real-time updates directly to the casebook, saving time and aligning stakeholders on the changes.

"Live UAT updates are a game-changer," said Gulati. "By providing feedback, fixing problems, and testing updates immediately, we can eliminate three to four weeks from our timeline."

By modernizing its clinical data management processes, Vertex has reduced average build time to 7.5 weeks, meeting its goal and continuing a track record of operational excellence.

Lotus Clinical Research: Streamlined Data Quality Reviews

In addition to being a full-service contract research organization (CRO) for analgesic studies, Lotus Clinical Research operates a state-of-the-art research site. It aims to lead the pain market

for CRO and site services by introducing and validating technologies that will improve analgesic study design and conduct.

The company adopted an EDC solution that was easier to use for site personnel, data managers, and clinical research associates (CRAs) and that improved efficiency across teams. With a capability in its EDC system that allows patient listings and forms formerly created for the use CRAs at a significant cost of time by data managers to now be automatically generated within the system itself, Lotus automates the tracking and sorting of patient data for entry, source data verification (SDV), and review.

"I used to send my monitors all the reports before they went on their monitoring visits," said Andrea Krueger, a data manager for Lotus. "Now my CRAs told me not to send them anymore, because [in our EDC now], you click on a subject casebook and it shows what requires SDV and what queries need to be addressed. It's all in the system already."

This functionality provides benefits to data managers and CRAs, saving both monitoring time and effort. Instead of cross-referencing a spreadsheet, CRAs work directly within the EDC. The system filters out the visits and forms that haven't been completed or that were already reviewed, listing only the data that need SDV and queries that need answers.

Data managers can also save time preparing for meetings with clients. The reports and dashboards that show progress and status of data entry are also fully automated in the cloud-based EDC system.

"Our clients really like receiving the status reports," said Krueger. "They can see the status of SDV and data reviews, look at the query reports and status, and who opened and closed queries. The dashboards have saved me an enormous amount of time as well. Before, I would pull reports, calculate the metrics, and plug those into our template. Now, I've configured my dashboard to show that exact same data automatically. We simply pull up our dashboard during the sponsor calls and walk them through the status, and we can double click to drill down into any of the metrics if they have questions."

A user-friendly interface also makes data entry easy for clinical research coordinators. Automated task lists and interactive task-scrolling allows the site staff to complete their work more efficiently and with fewer errors.

"Our [system] gives site personnel a user-friendly interface that takes them directly to what's needed so they no longer have to click through casebooks and find where they left off," said Jennifer Nezzer, director of biometrics at Lotus Clinical Research.

Cara Therapeutics: Trial Data On Demand

As a small clinical-stage biopharmaceutical organization, Cara Therapeutics outsources its studies to CROs, often using different vendors for different studies. It's a growing trend in response to the rising complexity and cost of running a trial. It is estimated that by 2020, nearly three-quarters of trials will be outsourced to CROs.{3}

Outsourcing trials created delays in accessing data because the company was dependent on CROs to handle periodic exports of the data. Working with multiple CROs also introduced variability into the CRFs and datasets, creating more work downstream for the programming team because each CRO used its own EDC and standards.

Cara wanted the benefit of using CROs that specialized in specific clinical areas, while also maintaining control over CRFs. By providing CROs with a cloud-based EDC, Cara was able to standardize and align data collection from multiple CROs.

"Our new clinical data management system gives us control over our casebooks and consistency in our data when working with different CROs," said Evelyn Dorsey, associate director of data management for Cara Therapeutics. "We've used the system with more than five different CROs, and they have all been impressed with the speed of building studies and making mid-study changes."

Rather than waiting until the end of the month for data transfers from a CRO, now Cara can analyze and investigate data continuously by simply signing into its EDC. Cara has constant, direct access to its trial data in real time. With higher visibility into study status, it also sees the

operational reports showing the status of data collection and cleaning without having to ask the CRO for a separate report.

Flexible reporting within a cloud-based EDC is also valuable when working with multiple CROs. Sponsors see operational data in a consistent way across studies, while each CRO can see the study metrics and reports according to its own preferences.

"We have six or seven different CROs working with us, and they have three or four team members within the data management group working on each of our studies," said Dorsey. "Flexible reporting is really valuable to us, as we are able to share our custom reports from other studies as a baseline. Each team member with access to the EDC can customize their view of that report however they like it, without the need request such reports from the programming team, which also means cost savings for Cara."

EDC Innovations Advance Clinical Trial Efficiency

There are dramatic changes under way in clinical data management, and yet the challenges associated with EDCs and managing site data have persisted for years. The recent advancement in EDC innovations are helping companies like Vertex, Lotus, and Cara solve persistent challenges with lengthy build times, inefficient SDV, and disconnects between sponsors and their CRO partners.

Advancement in clinical data management will continue to help CROs, sites, and sponsors toward modernizing trial processes and reducing the speed and cost at which we can bring treatments to patients.

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GOOD MANAGEMENT PRACTICE

Hiring, Upskilling, and Retaining Quality Talent for Clinical Trials

Rocco Raffo; Taylor Crook
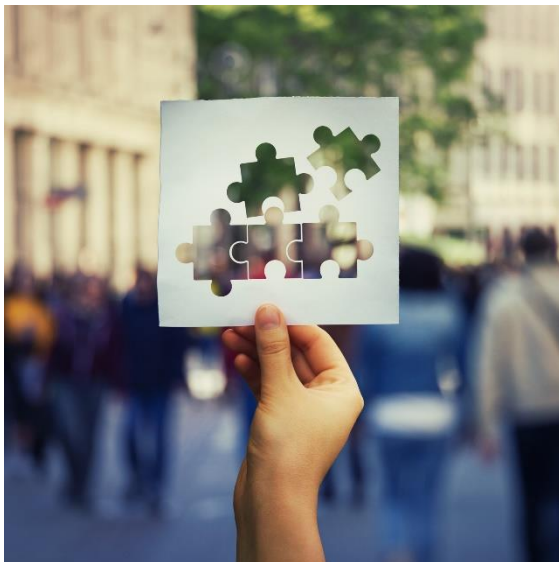
The U.S. life sciences sector in 2019 continues to be a leading driver of significant economic gains for the country, representing 2.1 million jobs across 82,300 companies last year. Buoyed by strong spending on research and development, the rise of biopharmaceuticals, and the increased healthcare needs of an aging population, the industry is taking advantage of the momentum built up over the past decade. This growth has led to an increased demand for clinical trials staff, which can be difficult to fulfill in today's labor market.

How do employers ensure they're making quality hires while controlling costs and supporting the complex, heavily regulated, long-term process of clinical trials? We offer recommendations to mitigate three critical challenges facing employers: finding qualified candidates, overcoming the skills gap, and increasing retention.

The Industry Landscape

First, a little perspective on the industry. Globally, there are more than 312,000 open clinical trials, up from nearly 83,000 in 2009 (an increase of more than 275%). This aggressive growth has also driven additional merger and acquisition activity, the expanded use of functional service providers and contract research organizations, and even more funding and investment. In the first

quarter of 2019, at least 30 life sciences companies announced new efforts such as expansions, new locations, increased funding, and new trial and product launches.

The talent shortage has forced many employers to pay more to compete with other companies seeking the same talent, driving wages up dramatically, which is painful in the short term and unsustainable in the long term. "Life sciences industry wages are higher and growing faster, on average, than those for the overall economy," according to JLL. "Median wage for life sciences occupations, according to the Bureau of Labor Statistics in 2018, was more than 70% higher than the national average of all other occupations."

Finding Qualified Candidates

The twin challenges of a limited and expensive talent pool may threaten growth in the life sciences sector. The tension between supply and demand has clinical trial sponsors experiencing slower "time-to-hire" processes and higher turnover, both of which have negative effects on productivity, timelines, and progress.

One approach employers can consider is being more flexible with talent experience minimums. The industry has recently begun to realize the unintended consequences of its overemphasis on the experience requirement; companies are increasingly investing in people with a certain degree of competencies as opposed to a specific number of years in the profession.

The Association of Clinical Research Professionals (ACRP), for example, has begun collaborating with various organizations to promote the elimination of the "arbitrary" requirement for entry-level clinical research associates (CRAs) to have two years of monitoring experience, which has nearly "eliminated the CRA pipeline and resulted in an ongoing shortage of new entrants to become CRAs." ACRP contends the industry focus should be on developing "clear descriptions of core competencies and skillset expectations [that] will benefit both employees and supervisors."

Overcoming the Skills Gap

The key is finding great people. If you're recruiting high-quality candidates, you are more likely to succeed in training new hires on the specific needs of each workplace.

Two vital skill sets—one for clinical research coordinators (CRCs), who organize the research lab and interact with study participants, and one for the aforementioned CRAs, who visit clinical trial sites to monitor compliance with Good Clinical Practice guidelines—are in especially high demand.

CRCs need to be extremely organized and comfortable moving from task to task. They need to work at a high level with both data and people, navigating strict guidelines for patient eligibility criteria, monitoring and reporting results, and increasing awareness of clinical trials. They have a critical responsibility to ensure compliance and avoid risk. They need to be tech-savvy in order to work in multiple systems.

CRAs also need to be able to comb through reams of technical medical data, with a focus on identifying and addressing any potential problems. They need very sharp critical thinking skills and the ability to travel to various research sites.

Because of these factors, there are other jobs that prepare workers well for a switch to CRC and CRA careers. Consider recruiting from other health-related positions, including:

- Radiation technicians
- Phlebotomists
- Medics
- Medical assistants
- Licensed practice nurses

In the future, as upskilling becomes more commonplace in helping to build the talent supply, we may also find employees outside the life sciences industry who have transferrable skills and competencies. Especially as life sciences becomes more automated, we may look to other

industries such as banking and finance to find additional candidates who have skills in critical thinking, analysis, multitasking, risk aversion, and customer care.

Double Down on Retention Strategies

Boosting retention is always a good idea, but the current labor market makes it even more crucial. Upskilling—training and advancement practices that help workers learn new skills and take on new responsibilities—has gained increased interest from companies navigating today's tight hiring market, and with good reason. It's a long-term view that ensures your employees have the skills needed to lead you into the future and assist with your company transformation. Identify the skills that will be most valuable in the future and provide the training and technology-enabled learning that could help them, such as digital skills and/or product development.

It sounds simplistic, but implementing consistent and relatively frequent performance reviews also goes a long way toward keeping employees engaged and on track. Employees want to know where they stand in the organization and opportunities for improvement, and they don't want to wait a year to find out. In addition to weekly or monthly meetings, consider "feedback in the moment," which is a great way to quickly reinforce good behavior and address negative behavior.

For many workers in life sciences, the most important driver of satisfaction is feeling valued; knowing that their work is contributing to the company and to society. They want to be involved in something that really helps people. Participating in breakthrough research or helping a new medication or treatment get to market where it could cure illnesses or even save lives is a powerful motivator.

This is a key component of an organization's employee value proposition (EVP). However, company leaders also need to ensure their EVP aligns with their brand, so employees can select a company that aligns with what they are looking for. Although it may seem as if all candidates might prefer to work in a large, well-known company, some candidates might prefer a small, more hands-on atmosphere that will grant them additional opportunities to make their mark and get more responsibility.

Conclusion

As they struggle to fill critical positions in a timely way, employers may be tempted to choose expediency over quality. However, any missteps in compliance risks compromising patient safety, draining the budget, and harming companies' reputations. For employers and staffing partners, that means balancing sometimes-competing goals:

- Quality
- Volume
- Time
- Cost

The cost of disruption cannot be overstated; people's lives depend on drug trials. Any staffing gaps can impact the lives of patients.

Successfully building and retaining a high-performing workforce demands a future-oriented mindset. Clinical trials and drug development are costly; you want to make sure you're considering all key factors in how you approach your hiring, upskilling, and retention strategy.

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RECRUITMENT & RETENTION

Book Opens the Universe of Patient Engagement to Trial Volunteers and Professionals

With the insight of a thought leader and the perspective of a historian, Kenneth Getz has been a keen observer and important contributor to advancing clinical trials for many years. He's just published the third edition of his popular book, "The Gift of Participation: A Guide to Making Informed Decisions About Volunteering for a Clinical Trial." *Clinical Researcher* Editor-in-Chief Michael Causey talked with Getz in late September on a wide range of topics, some of which were first presented in [a recent ACRP blog](#).

In part one of the conversation, Getz discussed the ongoing evolution of patient engagement in clinical trials. In this segment, he describes how market demand compelled him to update the book, and how it helps fuel the overarching mission to deliver high quality clinical trials to patients everywhere.

You're like James Brown, the busiest man in clinical trials show business out there. So, what compelled you to make the time to do this? Because writing a book takes time.

Getz: I wrote the first edition in 2009 and it was written out of just growing demand. We were getting so many calls, so much interest from people who were thinking about clinical research—people who have been recently diagnosed and a clinical trial appeared to be a good option for them. And I just felt that if we could package a lot of good tips and pointers into a reference manual of some sort—one that's just really written in plain language—that that would have some value and interest to people and to patients, and the book really took off. But since we first launched that early edition, the book has sold or has in circulation a total of about a quarter of a million copies.

For a very niche oriented publication, it just shows you the kind of demand and interest that's out there, and we see this play out every time we have an educational event. Where we'll see people who just come out of curiosity, not even for a health reason. They've just come to learn more because they see or hear an ad on the radio or they see a billboard on the highway or in the newspaper, and they want to just become more educated.

I think anybody not named Stephen King would be pleased to have anything close to those sales numbers. There's obviously a need for and interest in this book.

Getz: And you know, that was an important part of the initiative, too. All of the proceeds from the book cycled back into CISCRP's* other educational initiatives, so it's another way to tie all this together. Interestingly, the very first edition of the book was recognized by the editors of the Merck manual. They then contacted me and asked me to write a chapter in the Merck manual on a clinical trial. So I adapted some of the material from "The Gift of Participation." And a lot of this content also has taken on a life of its own and is appearing in a lot of other places. The Michael J. Fox Foundation has used some of the content from earlier versions of "The Gift of Participation," and that's really good to see as well.

How much has changed in the book in the last five years?

Getz: Between the first and the second edition there were changes, but in many cases I just added some supplemental paragraphs to existing chapters. This is the first edition where I really,

completely revised the flow and rewrote whole sections and created a number of new chapters, most notably the one on patient engagement.

This new edition actually does talk about what the future might look like under patient-engaged clinical trials. The very first edition didn't touch on any of this. I mean, it was 2009—it was sort of pre patient-centric clinical trials and patient-focused drug development, so before many of the initiatives that have come to help stimulate the development of more support for patient-engaged trial participation. The next edition, the second edition, touched on a few areas where we were really starting to see changes. The introduction of wearable devices and home nursing networks, for example, but it was still very, very early days.

This new edition puts all of this into its own chapter and talks about why this is such an incredibly exciting time for patients to be participating in clinical research. Because there's so much focus on partnering with the patient, on improving convenience, on giving patients a voice in protocol design and helping to define clinically meaningful outcomes for the trials. Also in the return of trial results and the disclosure and transparency of what we learn in our studies, and in the role that broader data and analytics are playing and how we're engaging stakeholders that have often been outside the research enterprise. And how they're being engaged more actively, including by health systems and healthcare professionals, and even as payers in the whole clinical research enterprise.

The idea that you could participate in a clinical trial right at the point of care and throughout your own health journey [is a new concept]. So that's more forward looking—the idea of the learning health system, where every time you take an over the counter medication or a prescription drug, whether it's approved and commercially available or it's an investigational therapy, something is learned about your response. And that ultimately is aggregated to inform our understanding about population health and how people are responding to different therapies and treatments over their own health journey over the course of their own lifetime. "The Gift of Participation" frames so much that has happened over the last five or six years and talks a bit about the promise that it holds for the future.

It's interesting you bring that up as a topic as one of the things I want to focus on, partially riffing off the title of the book itself, but I think sometimes in this industry we don't always appreciate the patients. We don't really appreciate the efforts they make or we can overlook their role. So talk about what does the title "The Gift of Participation" mean to you? Why did you select that as a title?

Getz: It's such a great question because it really goes back to the creation of CISCRP itself, which occurred in 2003, and looking for a language or phrases that would convey our appreciation and our admiration for people who decide to participate in clinical research—most often to benefit others. Because the vast majority of trials provide no benefit directly to the volunteer. And so "The Gift of Participation" was, in very simple language, a phrase that we used to really try to reorient our thinking about the heroes—the people who make the choice to help improve our overall knowledge of disease and how to treat it. The people who make decisions to act in ways that may bring no personal benefit to themselves, but bring benefit to others. And that's truly a gift that they give.

*Proceeds from "The Gift of Participation" fund educational programs of the nonprofit Center for Information and Study on Clinical Research Participation (CISCRP), for which Getz is founder and chair in addition to being deputy director and research professor at the Tufts Center for the Study of Drug Development. To find out more, go to https://ciscrp-educational-resource-store.myshopify.com/products/the-gift-of-participation-a-guide-to-making-informed-decisions-about-volunteering-for-a-clinical-trial.