ACRP

FOR LEARNING FOR LISTENING FOR LIFE

Clinical Researcher™

The Authority in Ethical, Responsible Clinical Research

March 2021 (Volume 35, Issue 2)

Does the World Recognize the Clinical Research Professional in Your Mirror?

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Clinical Researcher™

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EXECUTIVE DIRECTOR'S MESSAGE

Ensuring Our Workforce Foundation is Firm

Jim Kremidas

I'm excited that this month's issue of *Clinical Researcher* focuses so much on the clinical trial workforce. The work you do is the foundation of our success as an industry. Never has this fact been more apparent than in the past year, as thousands of clinical trial workers at numerous enterprises have worked together and separately to develop pandemic-fighting vaccines in record time.

At ACRP, we believe firmly that the best ways to advance the quality and efficacy of clinical trials are to further professionalize the workforce with training, to establish meaningful and transferable competencies and standards, and to develop tools to certify and validate work performance.

As an industry, I'm happy to report we are making great strides in this direction. For example, the Partners in Workforce Advancement (PWA) initiative continues to gain exciting momentum. The PWA is a multi-stakeholder collaborative initiative to grow and expand the diversity of the clinical research workforce, and to set and support standards for workforce competence.

The PWA's ranks are growing; earlier this year, we announced Javara had joined us. Late last year, we welcomed Altura and Wake Forest University. Currently, we have nearly 30 members representing a wide spectrum of clinical trial activities. Watch this space for more announcements!

ACRP also launched an important Diversity Advisory Council (DAC) in January. With the understanding that it is well past time to diversify the patient population, ACRP joins other leading organizations in recognizing a key to attaining that lofty goal is to diversify the clinical trial workforce.

The DAC will recommend strategies to recruit and retain clinical research professionals and students from historically underrepresented groups with the goal to enhance the quality of the existing workforce, as well as improve the overall climate of inclusivity, communication, and cultural understanding across the field. Again, watch this space for progress reports in the months to come.

As always, thank you so much for what you are doing to promote health and prolong life. I can't think of a higher calling, and it's our honor at ACRP to support your efforts in any way possible.

If you have thoughts or questions about ACRP's activities, please reach out to me at jkremidas@acrpnet.org.

Jim Kremidas is Executive Director of ACRP.

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CHAIR'S MESSAGE

The Professionalization of the Clinical Trial Industry

Erika Stevens, MA

Does the clinical trial industry need to do more to professionalize itself?

While the clinical research enterprise aids the development of novel clinical therapies, the occupations supporting these roles are unidentified by the Bureau of Labor Statistics (BLS). Neither clinical research associates (CRAs) nor clinical research coordinators (CRCs) are classified by the BLS. Members of ACRP, however, readily recognize these key roles and others as parts of the workforce keeping complex clinical trials moving safely and efficiently throughout the clinical research lifecycle.

Whether officially recognized by the BLS or not, CRCs, CRAs, and others perform critical tasks enabling the advancement of new healthcare treatments; yet the lack of recognition by the BLS impedes the industry in defining critical metrics, such as the size of the workforce or hiring trends.

ACRP is leading the way in raising awareness of this problem and offering some possible solutions. Among these efforts are initiatives aimed at defining key roles within the clinical research industry, mapping the competencies for job performance, providing education/training critical to these jobs, and validating clinical research workforce capability. We also need to work toward establishing greater standardization through the industry to help attract new talent, while at the same time retaining among us the best and the brightest.

ACRP will continue to be a catalyst committed to elevating the clinical research workforce both in terms of performance and as a profession. ACRP is committed to educating leaders in government and to partnering with professionals at the National Institutes of Health and other organizations to advance clinical research certifications. As Chair of ACRP's Association Board of Trustees for 2021, I am dedicated to supporting these initiatives to drive the professionalism of the clinical research industry.

I look forward to working closely with you, the members of ACRP, on these and other exciting endeavors the rest of this year and beyond.

I wish you all the best jusqu'a la prochaine fois (until the next time),

Erika Stevens, MA, has more than 20 years' experience in the research industry, is the 2021 Chair of the Association Board of Trustees for ACRP, and leads Transformation Advisory Solutions for Recherche Transformation Rapide. She advises life sciences companies, health systems, academic medical centers, foundations, hospitals, and contract research organizations in process improvement initiatives for quality and efficiency in operations, cross-functional relationships, administration, manufacturing, and compliance. Her earlier volunteer duties with ACRP include service as Chair of the Editorial Advisory Board, a member of the Conference Planning Committee, and President of the New York Metropolitan Chapter.

Clinical Researcher—March 2021 (Volume 35, Issue 2)

PEER REVIEWED

Are Clinical Research Coordinators Recognized as Professionals?

Erika Stevens, MA; Liz Wool, RN, BSN, FACRP, CCRA, CMT

As the number of global clinical trials continues to rise, so does the need and demand for qualified research support personnel, which further drive expectations for clearly established job functions. Variability in the assigned roles and responsibilities among clinical research coordinators (CRCs) creates opportunity to provide clarity in defining the profession.

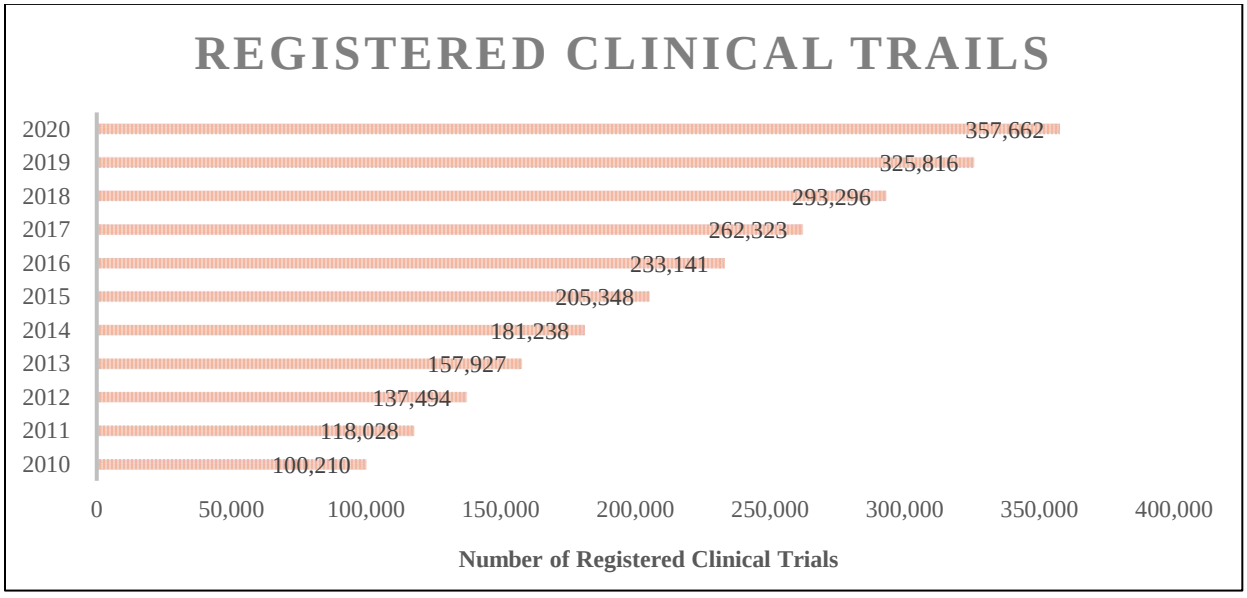
This article identifies the gaps in industry recognition and classification practices for CRCs. Understanding national demographic benchmark trends among CRCs and clearly defining position expectations will provide insight into the professionalization of the CRC position. The ability to establish a clearly defined career roadmap for the CRC—one based on a thorough understanding of the role's salient competencies—better enables job performance and provides opportunities for career advancement and credentials to those in the profession.

Background

The CRC (also referred to as clinical trial administrator, research coordinator, and other terms) role is not described or defined in regulations or in the Good Clinical Practice (GCP) E6 guideline of the International Conference on Harmonization.{1}

Although the field of clinical research continues to grow in the U.S., with the number of clinical trials having more than doubled in the past 10 years{2} (see Figure 1), much of the workforce supporting this growth remains unrecognized by the Bureau of Labor Statistics (BLS).{3}

Figure 1: Registered Trials on ClinicalTrials.gov, 2010–2020 (as of November 12, 2020)



While absent data on CRCs, BLS published an article on occupations in biotechnology referencing CRCs, describing their primary functions as recruiting and screening patients who try new treatments and monitoring and reporting on patient progress.{4} As of 2019, medical scientists and clinical laboratory technologists/technicians are recognized and tracked in the annual occupational outlook handbook from the BLS, but absent still is a CRC listing. Medical scientists are defined as those who "conduct research dealing with the understanding of human diseases and the improvement of human health; engage in clinical investigation, research and development (R&D), or other related activities."{5} Meanwhile, research managers, research

analysts, and survey researchers make the list, but their definitions do not address the competencies required for the role of the CRC.

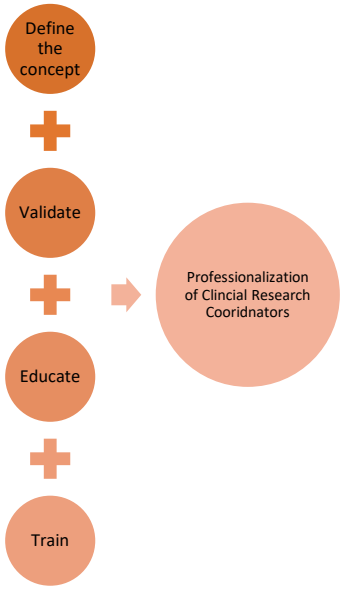
Arguably, understanding human diseases, improving health, and engaging in clinical investigation and R&D could fall under the purview of the CRC. While the BLS does not recognize CRCs, various membership-based organizations recognize clinical research personnel within the field of clinical research. For example, the membership of the Association of Clinical Research Professionals (ACRP) includes CRC as the largest specialty role represented in its ranks. Still, how does the occupation of the CRC become one that is recognized officially as a profession by regulatory authorities and other levels of government?

In Search of Professional Recognition

The first of four steps (see Figure 2) is to define the concept by aligning similar organizations into a common industry. Webster defines industry as, "manufacturing activity as a whole and [an activity] that employs a large personnel and capital especially in manufacturing."{6} Similarly, the BLS defines industry as "a group of establishments that produce similar products or provide similar services."{7} In this case, aligned organizations participating in clinical research would be classified as functioning within the clinical research industry.

Broadly defined, those who "engage in clinical investigation and R&D, or other related activities" are part of the clinical research industry—this includes executives, staff, and vendors tied to sponsors of studies (from pharmaceutical, medical device, biotech, and biologics firms, independent principal investigators acting as sponsors, patient recruitment specialists, contract research organizations [CROs], etc.), personnel at study sites (based in private healthcare practices, academic medical centers, health systems/hospital networks, site management organizations, etc.), and relevant employees in regulatory bodies (e.g., the U.S. Food and Drug Administration, Office for Human Research Protections, Centers for Medicare and Medicaid Services, etc.).

Figure 2: Steps for the Professionalization of CRCs



Thus, a wide swath of what may to the uninitiated seem to be only loosely related organizational occupations fall within the clinical research industry. The BLS allows for a given industry to have employees in dozens of occupations,{7} and leverages the North American Industry Classification System coding structure to group establishments together based on their primary activity and those with similar labor into 20 industry sectors.{8}

The next step in validating an occupation is to define the responsibilities directly related to the job role. In a presentation leveraging two national CRC datasets from the Clinical and Translational Science Award (CTSA) Research Coordinator Task Force, Speicher et al. present evidence of tasks well outside the original defined scope of clinical trial management.{9} Later, Speicher et al. published results of the CTSA's CRC survey indicating the roles and responsibilities assigned to CRCs are vast and not clearly defined.{10} Many of the tasks identified in the results align with those defined by BLS as "participating in clinical research investigation."

The defined competencies for the clinical research professional remained unclear until the Joint Task Force for Clinical Trial Competency published its competency domains for clinical research.{11} The task force outlined the knowledge and skills required throughout the clinical

research enterprise and, in May 2018, ACRP published core competency guidelines for the CRC, identifying entry-level, mid-level, and senior-level competencies and tasks.{12} Competency models solidify required knowledge and mastery of tasks within an industry, providing detailed information about job requirements and proficiency.{13} Identifying and mapping the required skillset needed to perform the expected position enables assessment and confirmation of acceptable performance for the assigned job/role.

Many industries use education as a pathway for the levels of comprehension and ability necessary to perform job-based requirements. In the same career outlook article on jobs in biotechnology, BLS recognizes most CRC jobs require a minimum of a bachelor's degree and in some positions a master's degree.{14} A variety of academic programs offer industry-specific diplomas or degrees specializing in the field of work, and educational opportunities to support clinical research continue to expand. The Consortium of Academic Programs in Clinical Research (CoAPCR) lists 51 clinical research academic programs.{15} Leveraging the CRC competency model criteria, educational programs can more clearly align curricula to specified job functions.

A recent snapshot of the ACRP member database shows that 43.26% of respondents to a request about educational attainment hold a bachelor's degree as their highest level of achievement, while 43.73% have one or more graduate degrees (see Table 1).{16}

Table 1: Reported Highest Level of Education of Responding ACRP Members in 2020

Highest Education	**Count**	**% of Total**
High School Diploma	259	2.64%
Associate/Two-Year Degree	650	6.63%
Bachelor's Degree	4,260	43.26%
Master's Degree	3,095	31.57%
Doctorate Degree	1,192	12.16%
Paraprofessional Diploma (LVN, medical assistant, etc.)	347	3.54%
Total Respondents	**9,803**	**100%**

Following education, the pathway to professionalization often requires certification, licensing, or credentialing. Certification supports the mastery of a specific skillset that is aligned to the job. “A certification is a credential that you earn to show that you have specific skills or knowledge. They are usually tied to an occupation, technology, or industry. Certifications are usually offered by a professional organization or a company that specializes in a particular field or technology.”{17}

Professions requiring certifications/licensing are arrayed across many industries. In 2018, more than 48 million people reported that they hold an occupational license or certification.{18} While some employers require certification for clinical research positions, certification is not mandated throughout the industry. Still, data support increased trial performance with certification.{19}

Haeusler’s analysis of four retrospective multicentered trials combined ACRP’s principal investigator certification (CPI) and CRC certification (CCRC) as evidence of Good Clinical Practice training and reported significantly fewer protocol deviations among those certified.{20} Nearly 10 years later, Hodges and Akroyd’s study reported fewer protocol deviations among CPIs and suggested a requirement for principal investigator certification may improve data quality in clinical research.{21} Further, in a 2018 Drug Information Association meeting, Tufts, ACRP, and the WIRB-Copernicus Group presented data analyzing 7,000 active CRCs, finding those with ACRP certification have fewer protocol deviations compared to their non-certified peers.{22}

While the evidence supports improved clinical research performance with certification, we reiterate that neither the clinical research industry nor its regulators currently require certification. At any rate, ACRP’s exam-based CCRC program is accredited and has produced more than 20,500 certificants in its 28-year history.

Arguably, certification supports the pathway to professionalization for CRCs by virtue of being a data-validated measurement of CRC capability. An Association for Clinical and Translational Science assessment of training for CRCs identifies a gap in certification and recommends a

formal assessment.{23} In a recent review of the literature, Bocchino et al. suggest that a blending of competency and performance outcomes may be required for assessing job performance.{24}

The roadmap to attain a BLS ranking for the CRC is well defined, and the research industry has collaborative work to do to achieve the goal of having the CRC recognized as a profession. Detailed in Table 2 are the requirements to be recognized as a profession by BLS.

Table 2: BLS Requirements and Clinical Trials Industry Status

BLS Requirement	Status in Industry	Explanation
Pay	Not uniform in the industry. Data available from ACRP.	Median data for wage and salary workers. Includes the top 10% and bottom 10% of the workers in the occupation.
Typical Entry-Level Education	Not uniform in the industry.	What is required to enter the workforce for occupation.
Work Experience in Related Occupation	Not uniform in the industry.	Transferrable knowledge and skills. Common substitutes for formal types of training or education.
Other Experience	Not uniform in the industry.	Experience in volunteering or while in school that can aid in attaining the job.
Important Qualities	Not uniform in the industry.	Skills, aptitudes, and personal characteristics.
Certification, Licenses, Registrations	Not required to get a job as a CRC.	Are any of these needed for the occupation. If it is needed, how does the worker attain?
Work Environment and Workforce Schedules	Not uniform in the industry.	Working conditions, typical workplace, level of physical activity, working hours.
Work Performed	Detailed job descriptions are not uniform in the industry publication by Speicher et al.{10}	Responsibilities, duties, and tasks; who the CRC interacts with; and frequent technology used.

BLS Requirement	Status in Industry	Explanation
Training and On-the-Job Training Needed to Attain Competency	Not uniform in the industry.	Post-employment classroom and on-the-job training needed for the occupation. Internships and apprenticeships are addressed in this section for job training. Competencies published by ACRP, Society of Clinical Research Associates (SoCRA), and Multi-Regional Clinical Trials Center of Harvard.
Advancement	Not uniform in the industry.	What is required for advancement in the occupation (e.g., certification, formal education). Also, opportunities for advancement can come from within an organization (becoming a manager or supervisor, for example).
Number of Jobs	Needs to be compiled from various sources.	Employment, or size, of the occupation in the based year of the employment projections.
Job Outlook	Needs to be compiled from various sources.	Projected percentage change over a decade. Job prospects for people to enter the occupation with information about how easy or hard it is to enter the occupation.
Employment Change	Needs to be compiled from various sources.	Projected numeric change in employment over a decade.
State and Area Data	Needs to be compiled from various sources.	Sources for employment, wages, and projections data by state and area.

BLS Requirement	Status in Industry	Explanation
Similar Occupations	Needs to be compiled from various sources.	Does another occupation have similar job duties or similar required skills?
More Information	Needs to be compiled from various sources.	Provides links to associations, organizations, and other institutions that provides readers with additional information.

In order to define each of these areas in a uniform manner to be recognized as a profession by the BLS, the research industry needs to form a CRC Professionalization Workforce Alliance comprised of various professional associations (e.g., ACRP, SoCRA, Society for Clinical Research Sites) and sites (e.g., government, non-government, networks, etc.). This alliance would agree upon, promote, and implement the BLS requirements in order to demonstrate standardization of the CRC role in the research industry. This requires our industry to break down the "silos"—each stakeholder's niche in the industry—for the greater good of having our CRCs recognized as professionals. This alliance would also provide the future framework and approach for the industry to collaborate on the professionalization of other roles, such as the site monitor/clinical research associate.

Summary

The clinical research industry is well positioned to align sites, sponsors, CROs, and other organizations supporting clinical research to clearly develop the roadmap for the professionalization of the CRC role. Leveraging the work of the Joint Task Force for Clinical Trial Competency and ACRP's CRC core competencies defines the occupation. Industry-specific education and training provide the foundation for meeting the tasks assigned to the CRC role. Quantifying competency and confirming comprehension are garnered through assessment. The professionalization of CRCs relies on the culmination of these steps as referenced in Figure 2. As an industry, we are well positioned to implement the necessary training and to confirm the comprehension of defined competencies that will the catalyst for eventual BLS classification and recognition of CRCs as professionals.

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PEER REVIEWED

When the Phases are Exhausted

Preethi Sriram, DHSc, MSN, BSN

The approval process for new drugs in the United States is designed to be rigorous, and the U.S. Food and Drug Administration (FDA) provides oversite and monitoring of the overall process through regulations and guidelines in order to ensure that new products are both safe and effective once made available to the general public. In order to accomplish this, the FDA requires those developing new drug products to conduct safety and efficacy studies in an exact manner.{1}

After preclinical studies are conducted, the different phases of clinical trials in human subjects are Phase I, II, and III before any approval and marketing of a new drug product, followed by the possibility of Phase IV postmarketing studies.

Portney and Watkins{2} describe the preclinical phase as happening in laboratory settings, often in animal models, before a drug is tested in humans. Phase I is described as when researchers start experimentations in humans to collect data on the dosage, timing, and side effects of the drug, and is usually conducted on a sample set of subjects that range from 20 to 80 participants who may be healthy or, as is often the case for oncology drugs, may have the indication of interest. Phase II comes next in a larger set of participants who are always patients if the therapy has been shown to be safe in Phase I, and this is when the drug is studied to demonstrate its efficacy. Phase III studies are randomized, double-blinded experiments that compare the new drug with the standard of care or placebo, and these trials usually involve the largest subject populations, ranging from hundreds to even thousands of participants. Phase IV studies are

described as taking place after the drug has been approved, when the researchers may continue to investigate its effects in cases of other therapeutic indications or in different populations than those involved in the original trials.

Considering the Options

When a patient with a difficult-to-treat condition is not enrolled in a clinical trial due to not meeting the criteria of the study, or when there is no trial available for his or her specific disease, it may seem that there are few options left regarding cutting-edge treatment. The remainder of this article discusses lesser-known avenues to enrollment in clinical trials, the possibilities for using repurposed drugs that are already on the market for some other condition in off-label circumstances, and details of how compassionate use or expanded access studies are managed.

Access to Clinical Trials

In situations of rare diseases/terminal illnesses, it is important to know what treatment options are available for individuals apart from current standard of care, including the options within clinical trials.

Unger et al.{3} notes there are four barriers with regard to clinical trials—structural, clinical, physician, and patient barriers—expanded upon here with more detail:

- **Structural barriers** occur when a patient who would otherwise be willing to participate in a clinical trial finds that none are available for his or her condition at a particular treating institution.
- If a trial is available and the patient is assessed for eligibility but excluded due to not meeting the inclusion criteria, this is a **clinical barrier**.
- A **physician barrier** occurs if the patient would be eligible for a study but his or her physician never mentions the study, essentially taking the choice away from them.
- **Patient barriers** may include factors related to treatment preferences, transportation- and work-related challenges, income and insurance levels, family and peer pressures, religious beliefs, and other considerations.

A study by Carey et al.{4} found that the major barrier to trial participation is that potential participants are not invited to be screened for studies. Meanwhile, Duma et al.{5} conducted a review on cancer clinical trials conducted from 2003 to 2016 and found that, from the 1,012 trials reviewed, only 310 (31%) documented the ethnicities of the 55,689 total participants in those studies. It was noted by the authors that, when ethnicities were recorded, participation varied by ethnic groups and that non-Hispanic whites were more likely to be enrolled than African Americans and Hispanics. Another finding from the review was that subjects younger than 65 years of age had a higher likelihood of being enrolled than the elderly. Low recruitment was also noted amongst females compared to males. The authors note that most of the trials included in the analysis were completed between 2013 and 2017, and that the ratio of participation of minorities decreased following 2011.

It is important for both patients and providers to be aware of how to find clinical trials. One online resource on this topic{6} notes that a starting place is the website www.clinicatrials.gov, a registry of trials maintained by the United States National Library of Medicine at the National Institutes of Health (NIH) and holding registrations from more than 329,000 trials from 209 countries. Another resource{7} providing information for where to search for cancer indications notes that the National Cancer Institute's Cancer Information Service can provide a tailored search for clinical trials, and that many of the advocacy groups that exist for specific types of cancer maintain lists of relevant clinical trials or can refer individuals to organizations or websites that match patients to trials.

A resource for patients with rare diseases{8} notes that disease advocacy organizations have medical boards and services for physician locators and/or networks for patients, all of which can help in finding healthcare professionals who are familiar with specific conditions. Further, the Genetic and Rare Diseases Information Center helps patients find advocacy groups related to their specific conditions, and the Patient Recruitment and Public Liaison Office at the NIH provides information about participating in research at NIH hospitals.

It is important for healthcare providers to be aware of such resources as these as they seek to help patients find trials for which they may be eligible. Table 1 summarizes various resources that both providers and patients can utilize.

Table 1: Resources for Patient and Providers Who Are in Search of Trials

Source	Website/Contact	Summary
ClinicalTrials.gov	https://www.clinicaltrials.gov/	A database of privately and publicly funded studies conducted around the world.
National Cancer Institute (NCI) Cancer Information Service	https://www.cancer.gov/publications/dictionaries/cancer-terms/def/cancer-information-service 1-800-4-CANCER (1-800-422-6237)	This is NCI's link to the public for interpreting and explaining research findings in a clear and understandable manner, and for providing personalized responses to specific questions about cancer.
National Organization for Rare Disease (NORD)	https://rarediseases.org/for-patients-and-families/connect-others/find-patient-organization/	Lists free resources for patients and families affected by rare diseases. Organizations interested in being listed should contact membership@rarediseases.org.
RareConnect	https://www.rareconnect.org/en/communities	RareConnect responds to rare disease patients' need for information and connection by creating international online communities and discussion groups for specific diseases.
FDA.gov For Physicians: How to Request Single Patient Expanded Access (Compassionate Use)	https://www.fda.gov/drugs/investigational-new-drug-ind-application/physicians-how-request-single-patient-expanded-access-compassionate-use	When a physician wants to submit a Single Patient Expanded Access request to obtain an unapproved investigational drug for an individual patient, he or she must first ensure that the manufacturer is willing to provide the investigational drug for expanded access use. If the manufacturer agrees to provide the drug, the physician should follow

		the steps given to submit an Investigational New Drug application to the FDA.
Genetic and Rare Diseases (GARD) Information Center	https://rarediseases.info.nih.gov/diseases	GARD maintains a list of rare diseases and related terms to help people find reliable information.
National Institutes of Health (NIH) Patient Recruitment and Public Liaison Office	https://clinicalcenter.nih.gov/participate1.html 1-800-411-1222	Professional nurses answer questions and provide information regarding the NIH Clinical Center's clinical trials and associated topics. Both the general public and practicing physicians may ask for details on specific research studies and the criteria for patient referral.
Expanded Access for Medical Devices	https://www.fda.gov/medical-devices/investigational-device-exemption-ide/expanded-access-medical-devices	This page is intended to help healthcare providers and device manufacturers learn about expanded access options for medical devices and associated criteria and requirements for each.

Repurposing of Drugs for Off-Label Use in Clinical Settings

Fajgenbaum and Rader{9} note that repurposing drugs is faster and far more economical than starting development of a new drug from inception, as many targets for drugs are shared across different diseases. The authors also note that historically, there have been many notable success cases for drug repurposing, for instance sirolimus for lymphangiolyomyomatosis.

In another publication, Fajgenbaum et al.{10} note that the COVID-19 pandemic is the largest pandemic that has been seen in decades, yet in its early days there were no specific, FDA-

approved drugs for use in COVID-19 patients. The authors provide a systematic review of numerous off-label treatments for possible use against COVID-19.

Further, in his book, *Chasing My Cure: A Doctor's Race to Turn Hope Into Action*,{11} Fajgenbaum describes how an uncle of his was diagnosed with metastatic angiosarcoma. When asked if a sample of the tumor could undergo genetic testing, the healthcare provider declined, saying that such testing, in the opinion of the doctor, would only impact treatment selection in 10% of the population. The author delved deeper and requested that a PDL-1 test be performed, and if the test was positive, that the doctor consider treating his uncle with an FDA-approved PD-L1 inhibitor or its receptor. The provider's response was that, even if the test was positive, the drug most likely would not work and would be expensive. In the uncle's course of getting a second opinion, an oncologist performed a genetic test that found the cancer cells were positive for PD-L1. The author's uncle was prescribed one of two already FDA-approved drugs for lung cancer and melanoma. After starting the drug, the uncle showed dramatic improvement in his symptoms, laboratory abnormalities, and tumors. Faigenbaum notes the particular case of his uncle receiving the drug has led to other off-label use of it, as well as to new clinical trials for the drug and drugs similar to it.

In many life-or-death situations, patient advocacy can benefit patients who do not have medical or healthcare backgrounds by helping them to conduct self-study on their therapeutic indications. It can also help them to seek guidance from trusted healthcare workers, or someone who is knowledgeable about their disease state, who can advocate for them regarding off-label use of a drug that is already on the market.

Compassionate Use/Expanded Access

In a memoir, *The Perfect Predator: A Scientist's Race to Save Her Husband from a Deadly Superbug*,{12} an American husband-wife couple writes about how the husband had become sick when vacationing in Egypt and was taken to a local hospital for potential treatment. From there, he was flown to a hospital in Germany, where a psuedocyst was discovered growing on his pancreas which had a bacterial strain of *A. baumanni* that is resistant to antibiotic treatment. He was flown back to America for further treatment and care, and his wife learned from her research

on the condition that certain viruses known as phages could be of use in such conditions. In an interview conducted by Corbyn,{13} the authors describe how phages were first discovered in 1917 by Felix d'Herelle, but he unfortunately had an arduous time getting the work accepted because he lacked formal medical training and was considered a "vagabond scholar."

The authors also describe in the interview with Corbyn that, after penicillin came to the market in the 1940s, phage therapy largely fell out of sight in the West during the Cold War but continued in Russia. While conducting this research, the wife, who is a colleague and friend of the chief of infectious diseases at UCSD School of Medicine, shared her findings with him, and he agreed that if she were able to find phages that matched the bacterial infection for her husband, he would contact the FDA and get approval for compassionate use of the experimental therapy. With help from a researcher from Texas A&M University, a phage was found that could be used against *A. baumanni*. The wife was also able to access another phage cocktail from the U.S. Navy, which was the treatment that ultimately worked in her husband's case.

While this example is heartening and shows a successful pathway taken in an extreme situation, it is important to realize that not everyone may actually get the off-label drug required for their condition in the same manner. For example, Rangarajan{14} describes having a daughter with a lysosomal storage disorder and how her physician followed the protocol of the pharmaceutical firm Shire for applying for compassionate use of one of its products in her case. The drug was already being tested in clinical trials, but the daughter was not eligible for them, and the company denied the request. The author notes that while there is, in theory, a "right to try" policy allowing those who are critically ill to go directly to the company and bypass the FDA, there is nothing forcing the company to take positive action in any particular case.

For the case of the patient or family advocating for expanded use, it is important to work with experts in the field and doctors who are willing to help in seeking FDA approval for trials or help in managing a pharmaceutical company's appeals process (see Table 1).

Devices vs. Investigational New Drugs

While the examples referenced so far have related to clinical trials of drugs and their off-label uses, similar concepts can be applied with regard to medical devices. Information from the

FDA.gov website{15} notes that expanded access is a potential option for patients with serious or life-threatening indications to gain access to medical devices that have not been approved for treatment outside research studies—assuming there are no comparable or reliable alternative therapy options available. The three options noted by the FDA outside clinical trials include emergency use, compassionate use, and treatment Investigational Device Exemption (IDE). It is noted that, while emergency use of an investigational device does not require FDA approval, compassionate use and treatment IDE do; all three require follow-up reports as well to the FDA (see Table 1).

Seeking Second Opinions

Katella{16} notes that Yale Medicine doctors often see patients who would like to obtain second opinions on their conditions but worry about insulting their primary doctors. Noting that truly professional doctors are not offended by such desires and that second opinions may be important in some cases—for example, in complex disease situations or when the treatment plan is unclear—Katella adds that the process can include getting a referral from the current doctor and determining if insurance will cover the cost. Further it is important to gather documentation on the patient's relevant medical history and the original doctor's reports to be shared with any secondary healthcare providers being consulted.

Conclusion

Clinical trials should be accessible by all people, regardless of racial/ethnic background, age, or gender; however, we can see from literature this is not always the case, especially for those who are racial/ethnic minorities, elderly, and females. In cases when patients are faced with rare diseases/terminal illness, it is important that the healthcare provider help the patient and his or her family seek potential options for appropriate clinical trials. If the patient is not eligible for a trial, or in situations when there is no trial that is available, the patient and family could conduct research into the therapeutic indication and seek expert consultation for potentially using drugs that are already available on the market for off-label use.

Table 1 summarizes resources that can be utilized in searching for trials and seeking further guidance for individual patients and their healthcare providers. In certain scenarios, the patient

can also look into potential options for trying to enroll in compassionate use studies of experimental drugs or devices through FDA approval or allowance by the company testing the product.

There are benefits and limitations to each of the options described in this article, and it is important for the patient and family to work alongside their healthcare provider in order to determine the next best steps for patient treatment and care.

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SPECIAL FEATURE

What Does Clinical Trials Success Look Like After a "Sink or Swim" Year?

Elizabeth Weeks-Rowe, LVN, CCRA

COVID-19 forced many unprecedented changes upon our day-to-day world—some of which still have us reeling. It has impacted our health, our economy, and our peace of mind. We don masks to guard against transmission; our body language becoming ever more an adjunct to communication limited by muffled words and hidden expressions. We wave through windows to neighbors and family members as our personal connections may put us at risk. In almost every way, "virtual" has replaced "actual" human interaction in our traditional workplaces and neighborhoods.

Meanwhile, an overwhelming "sink or swim" survival narrative has played in the background for the past year, amplifying our anxieties about the strategic choices available to us. Pivot or fail. Advance or retreat. Change or...die? The pandemic robs us of so many things, yet our ingenuity has remained steadfast and it will assure our survival as a society.

Beyond our individual home and office lives, COVID-19 impacted the core infrastructure of the entire clinical trials community with operational pauses at both industry and institutional levels. Stay-at-home orders resulted in studies halting, institutions furloughing, and brick-and-mortar offices uneasily transitioning to virtual workplaces to preserve safety. Everything and everyone was affected while ever-changing regulatory guidances complicated early efforts to rebound.

We had to develop effective alternatives to traditional study conduct to continue treating participants and to ensure credible data practices—all the while needing to limit exposure to the very people we want most to help. Telemedicine emerged as a viable replacement for non-critical study visits. Remote patient consenting facilitated preliminary screening efforts. The majority of investigational sites mandated administrative staff to work remotely, while clinical staff rotated shifts to ensure onsite study visit coverage.

There were radical alterations in traditional site management and monitoring practices. For example, video conferencing platforms have replaced in-person meetings and facilitated critical industry conferences. Further, remote monitoring/data review is the new normal, with institutions providing remote electronic medical record access to clinical research associates (CRAs) and sites using portals and/or electronic source systems to create/upload source documents for remote review. For many stakeholders, "virtual trials" and "patient centricity" have morphed from merely being buzzwords into their new status as successful elements of study design.

Sponsors, academic health centers, site management organizations, contract research organizations, patient recruitment firms, training organizations, independent consultants, and more—all levels and roles in the clinical research enterprise were forced to alter well-established processes to ensure business continuity amidst the fierce restrictions. This was a rapid-fire assimilation offering little time for adequate preparation, and yet our response to the devastation wrought was remarkably innovative. We accelerated activation strategies and reinvented execution to deploy investigational products and staff at "warp speed," resulting in sites opening in days and enrollment goals accomplished within months. The miraculous fruit of this collective effort includes several vaccines created and distributed in less than a year of the pandemic's first strike.

Sharing Our Successes

Through all of this turmoil, the clinical research community has once again demonstrated its passion to continue drug development, no matter the circumstances. The rest of this feature is devoted to examples (sometimes paraphrased for clarity) of successes that have arisen from the challenges, as graciously shared by a variety of experts in the field.

Joel M. Gelfand MD, MSCE, professor of dermatology, professor of epidemiology, vice chair for clinical research at the University of Pennsylvania's Perelman School of Medicine, and a principal investigator on the front lines of study patient treatment, describes the rapid adaptation to the pandemic that was necessary to continue critical studies in a large academic setting:

The COVID-19 pandemic has caused major disruption for clinical research. First, many academic centers have put institutional holds on any research not related to COVID-19. Second, there has been tremendous pressure on clinical research staff, who often need to balance work with increasing family demands, such as attending to their children's educational needs as schools go from in-person to hybrid learning to fully remote as the pandemic conditions spike.

Moreover, there is limited space to see research patients in person, as many centers are trying to move in-person care to telemedicine to maintain physical distancing in the clinics and waiting areas. To manage these issues, we have developed remote electronic tools so our coordinators can manage study patients without needing to be physically in the clinic. We now consent patients remotely and have remote coordinators manage many of our visits virtually. This approach reduces the demand on personal protective equipment, which is still in tenuous supply, lowers their risk for getting infected when commuting to work, and increases flexibility.

Meanwhile, with COVID-19 eliminating face-to-face meetings, clinical research training organizations and business owners were left scrambling to replace their classroom/conference educational curricula with a virtual equivalent that would still accommodate their diverse client base.

Liz Wool, CCRA, FACRP, president, chief learning officer, and chief learning strategist of Wool Consulting Group and the Wool Training Institute, describes a speaking engagement in early 2020 that was the catalyst for the changes to come:

At the end of January, as I watched what was emerging from China regarding the virus and tapping into my nursing background and experience in AIDS research in the 1990s, I cancelled my invitation to speak in-person for the Japan Clinical Trials Research Society on principal investigator supervision in early February 2020. This was, unbeknownst to me at the time, my first "pivot" that required adjustment, customer focus, and doing what it takes to keep my

commitment. This pivot ensured I delivered my presentation "live," but remotely, to the attendees in Japan—managing the meeting at midnight my time and conducting an on-camera question-and-answer session with the attendees.

"Pivot" became the theme for me and our team. When we pivot, we focus on what is most important at the time for each client and on providing solutions and timelines that sometimes result in less work for our team, but are still the right thing to do.

The pivots and clients' needs in 2020 also provided new opportunities. Our training services via eLearning grew and we shifted our live courses to interactive, engaging virtual training classrooms (not a webinar format).

Another result of the pandemic was the increased need for clinical researchers, due to the quick growth of the COVID-19 trial sector. Clinical research training programs, that were able to swiftly transform their core curriculum delivery, retained their clients and attracted new business in the process.

David Siberman, cofounder and CEO at Clinical Research Fastrack, a bootcamp training center that provides intensive education for professionals preparing to enter the clinical research enterprise, describes the rapid-fire curriculum delivery transformation required to keep his business afloat:

Our training program was completely in-person, hosted at eight locations around the country: Phoenix, Atlanta, Raleigh, Philadelphia, Chicago, Orlando, Dallas, and Austin. By the middle of March 2020, I knew my business might soon be on life support, with bankruptcy not far behind. I called my business partner and my National Program Director to share my fears. We could go down. Our entire business model was focused around in-person training. When the pandemic hit, everything had to change. Our survival was on the line.

We began by making several critical decisions. We would shift all our in-person classes to Zoom training. We started within our own team, offering coaching to help them find their inner strength and lead with optimism. We sent our team home to work remotely, providing information and guidance on how to effectively work and maintain sanity and productivity in the

home setting. We were in this together and would not lay anyone off, unless facing total insolvency. We told our staff to take whatever time and space they needed to cope during the crisis. We shared information transparently with our team, offering honest assessments of everything that was happening. At the same time, I offered a vision of credible hope and projected optimism. We cut all spending possible other than payroll.

We transformed our entire program to be delivered via video conferencing. The model that we had developed over the prior four years was completely re-created in just four days, and then we had 16 days of delivering 10 hours of back-to-back classes each day. Not a single student dropped from those sessions. In fact, extra students signed up because of the added convenience of training on Zoom. Our newly minted curriculum was at a higher quality than anything we had ever delivered and, shockingly, our students were getting hired out of class faster than ever before. Since then, we have focused on successfully helping hundreds of our students embrace new hope and begin fulfilling careers in clinical research.

Lastly, **Dan Sfera,** cofounder of The CRA Academy, describes the service changes implemented in his organization due to the pandemic and the positive outcome for students:

For the pandemic, we have switched our entire CRA Academy internship remotely. Students now monitor a breast cancer study completely electronically and submit their interim monitoring visit reports this way, as well. Many have been able to secure industry positions due to having this remote monitoring experience on their CVs.

It all goes to show how we continue the work no matter the obstacle in clinical research, swimming strong rather than sinking, because our passion for drug development leads us to pivot, refocus, and succeed.

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GOOD MANAGEMENT PRACTICE

Thoughts on the Care and Feeding of Your Organization's Future Leaders

Christine Senn, PhD, CCRC, CPI, ACRP-CP, FACRP, CSM

Many organizational behavior thought leaders—top among them today probably John Maxwell and Simon Sinek—have written at length about what it takes to be a strong leader, and, from what I've read, they're all right. Being a strong leader is a complex dynamic in which there are many possible characteristics, skills, and tactics one can choose to develop. There is no one set style or way of being that defines a great leader because we not only have to choose what is authentic to us as unique individuals, we also must embrace a style within the context of our company's culture.

I believe that chief among the key characteristics of a strong leader are knowing your own strengths and weaknesses, and having strong emotional intelligence so you hire people who work symbiotically together and who support the company's desired culture.

More specifically to clinical research leadership, however, I focus training myself and our company's managers on the following skills: setting expectations, providing quality feedback, and having difficult conversations.

Setting Expectations

People are not mind readers. What I have experienced as a psychotherapist (and from attending a few operas) is that misunderstandings can be devastating. How many fights have you had with a partner because of a misunderstanding? As an example, perhaps my definition of being on time for a date is that you arrive exactly at the time we discussed, but your definition is that you arrive no more than an hour late. There's going to be a fight!

I see managers make this error when they assume their employees are like them. I also see this error when managers have forgotten what it was like to learn their jobs. Managers have to constantly set reasonable expectations, coach their people on how to meet those expectations, and (as much as possible) ensure their people's success. It's a linear process comprised of setting up one's employee for many small successes to foster their sense of confidence.

A leader's role is a bit different. We do have to set expectations for anyone we manage, but I see a leader as being more of a mentor. (To keep *our* expectations aligned, I'll tell you what my definition of that is.) Anyone can display these leadership-mentorship behaviors.

A mentor gives very specific feedback on something done well, as a way of reinforcing that behavior. A mentor also gives very specific feedback on something that didn't go well, but with no malice or negative implications, just a learning opportunity. Mentors open themselves to being asked any question about anything in the company. When they don't know the answer to a question, mentors use the opportunity to teach employees how to find the solution. A mentor is in the business of directing people to resources, rather than giving them answers.

A mentor also demonstrates the company's values in everything he or she does. I don't think I've ever seen our CEO walk into one of our clinics without picking up a piece of trash that was laying on the ground in the parking lot, because—even if we share the building—it's a reflection on us. That might not be mentorship in your company, but we have a core value that Appearances Matter, so it's very much one of ours.

A mentor is someone who shows people a vision of what is possible. The vision I offer, for example, is to show others what implementing our CEO's vision well looks like: It looks like

meeting our clients' enrollment goals. It looks like amazing study startup timelines. It looks like phenomenal customer service by responding to our clients with grace and thoroughness. It looks like having a team of specialists who work together to ensure the highest quality data. It looks like collaborative teamwork that far surpasses anything you'd see on a motivational poster.

Every manager and every employee has his or her own vision. My opinion is that a leader's job is to not leave those visions to chance. Help people see the vision *you* want them to see, and show them that you embrace the greatness you want them to achieve.

SIDEBAR: Ingredients You Should Keep in Stock for a Strong Process Improvement Brainstorming Team

- At least one creative thinker, regardless of the person's role in the company.
- At least one person who knows the current process intimately.
- Two people who somewhat know the process but, more than that, embrace keen interest in process improvement.

In small companies, these can be overlapping people. In large companies, invite more people, but keep a balance as described above. Mix well and serve.

Providing Quality Feedback

Our industry is difficult to learn, with all its complicated regulations and procedures, puzzling acronyms, and scientific complexities. It's also an industry that few people have knowledge of before entering it. Given this environment, rather than annual reviews, I strongly recommend that any leader implement monthly reviews—whether just for his or her people or, if in a position to do so, the entire company. It sounds overwhelming at first, but such frequency offers many benefits, and having people do well at their jobs saves more time than monthly reviews take.

Monthly reviews help ensure your employee is exhibiting the soft skills expected for the job, is completing the tasks expected of the job, and is supporting customer service by showing your clients the best of your company. What is the damage done to your company if a client doesn't think you're responsive? If they think you're difficult to work with? What is the effect of not having people complete their tasks, and you not realizing it right away? We have had trials

where sponsor representatives have never sent us follow-up letters (despite our haranguing), and the project manager has had to tell us as the trial closed that, since the person responsible didn't do their job, we won't have any letters for our trial master file. That's not good for the sponsor or the site, and the U.S. Food and Drug Administration is not happy to learn of such situations.

There are simply too many moving parts in clinical research, and this is made all the more complex now with fast-moving COVID-19 trials. Going several months without verifying a person's work and documenting their accountability is a management mistake that can create vast leadership problems.

Having Difficult Conversations

Some people find difficult conversations to be frightening or rude. In fact, at least one study{1} suggests that nearly 70% of people avoid difficult conversations in the workplace. This leads to low morale, a toxic work environment, and damage to organizational performance and profit margins.

I follow the school of thought that every issue is either a "people" problem or a "process" problem. The only way to solve either one is to have an honest conversation. (The 70% of people who avoid these conversations are frankly not going to be good managers or leaders.)

The most critical tip is to always assume first that you have a process problem. Go into any situation wondering how to brainstorm the problem so that the process improves. I create many brainstorming meetings with people I think can contribute to improving the process. It's not the same people every time, because that would become stale; it's always people who either are creative brainstormers by nature, or who know enough about the process to think about how it could be done differently without becoming entrenched with their particular idea. Improving a process fixes nearly every issue.

If the process has been improved and most everyone is doing well with it, those who aren't are the problem. You have a couple of options here. If you avoid an honest conversation, you will watch the person continue to perform poorly, in which case you will ultimately terminate them

for poor performance, or they will leave because they feel like a failure. Your company or your department will suffer the entire time.

Instead, be brave. Have the difficult conversation with the person, and do so from a place of trust and acceptance. No matter how poor someone's performance, I've never met anyone who has done poorly on purpose. People genuinely want to succeed. They might make bad choices, but that probably means we didn't give them enough information to make good choices. They might prioritize tasks inappropriately, but that's on us as leaders for not sharing our vision with them.

If you go into these conversations truly believing that you and the employee have the best interest of the company at heart, then a difficult conversation isn't all that difficult. You're trying to help them save their job; you're trying to make you clients happy; you're trying to make the department or the company better. There's absolutely nothing negative in there, which is why I don't personally ever find a conversation difficult.

Worth the Effort

I'd like re-state that anyone and everyone can be a leader. There is no time like the present to train yourself how to set expectations, provide quality feedback, and have difficult (or shall we just call them honest?) conversations with your coworkers or your supervisor. These skills demonstrate leadership and can lead to promotions—and they usually have the extra bonus of bringing additional satisfaction into people's personal lives.

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SCIENCE & SOCIETY

Building on Experience and Being Driven by Compassion in Leadership

Al O. Pacino; Matthew Chandler

Now more than ever, we need to review what it means to be a leader in the clinical research enterprise. Many in the clinical research community are feeling pressured to produce innovative solutions while adhering to safety guidelines for COVID-19. Executives and clinical research leadership should be striving for the best leadership tools to ensure positive outcomes for all staff and patients. Executives should acknowledge the current circumstances of clinical research and inspire solutions from their staff to address challenges. Scientific and healthcare organizations, governments, and biotech companies should aim to improve their leadership capabilities by targeting key areas.

Creating a Culture of Empowerment in the Workplace

Many medical drug and device entrepreneurs know the impact of introducing innovations to the market that improve lives. They may have been involved with the co-founding, development, and selling of multiple start-up companies active in clinical research in their careers. In order to thrive in such a fast-paced environment, the most successful of them have learned that while it is common sense to keep an eye on the competition and identify possible partnerships, it is also critical to assess the workplace environment of their research staff.

Executives should be asking themselves whether they are applying their staff's strengths and mitigating any weaknesses. Making sure everyone feels listened to and valued is also an investment toward increased productivity and maintaining cooperation among teams. In practice, staff who feel a sense of self-empowerment are more inclined to improve processes and workplace attitudes.

Effective leaders also appreciate and act upon the importance of inclusivity and diversity in their organizations. Most major sponsors and biotechnology companies, and even the smallest of sites, know the benefits of having

a representative dataset. It's imperative that sites have access to the latest tools that target all demographics, so that the products and services approved in part through their efforts can be globally successful.

Collaboration at the workplace and business-to-business level will be crucial for long-term sustainability. One of the outcomes of having a collaborative work environment and industry is that the patient is a top priority. As our world becomes more and more interconnected, it's not only important to center the patient experience, but also to make sure we remain open to new ideas that may challenge our previous assumptions.

Managing Change and Adapting

Modernization is natural, and being knowledgeable of industry trends is just a first step clinical research executives can take. The time and expenses required to fully transition to modern and more efficient systems may seem too risky to undertake in today's clinical trials arena, but many of these new systems are worth examining.

For example, to this day, many stakeholders who participate in clinical research still rely on paper-based systems and silos that require many logins to conduct clinical trials at their sites. However, COVID-19 has demonstrated that digital solutions are becoming more vital to continuing the progress being made in the name of public health by the research enterprise. There is greater risk in not implementing a modern digital infrastructure, with the cost being the possibility of limited access to the latest scientific information and accurate data.

Meanwhile, different business models are becoming more readily available to executives and entrepreneurs that can ensure productivity, cohesion, and positive branding are maintained. Business models of the future will have to incorporate a level of cross-sectoral collaboration, minimize bureaucracy, and establish trust with the businesses' communities. Flexible business development plans can provide more beneficial opportunities to health training practices and patient care.

Further, it's imperative that clinical research executives stay dialed in to the ever-changing regulations that directly impact the industry. Governments, biotechs, and social media companies are continuously raising privacy and security standards to better protect individuals. It is essential that executives use their experience and judgement to identify laws that directly impact their research institutions.

Social media outlets are good tools to utilize and track new problems and new solutions being proposed throughout the clinical research community. Several influential clinical research executives, key opinion leaders, and patient-survivors routinely share their insights through sites like LinkedIn. Reading credible industry media publications can also inform decisions and necessary steps to address pending rules and requirements of clinical research.

Conclusion

Being in clinical research leadership can feel like an immense burden to some. The management philosophy and attitude executives carry into work every day set the tone for their organizations. Establishing a sense of shared responsibility can ease pressure and create more opportunities for staff members.

When it comes to continuing successful leadership, clinical research executives should consistently build their professional and business networks, while remaining committed to their goals and objectives for entering the field in the first place. Achieving and maintaining a productive and accountable work environment depends on everyone's mindset and ultimate desire to help patients.

Success is found in creating a workplace culture of self-empowerment, incentivizing collaboration, and understanding the needs of research stakeholders and regulators. It's time to use our increasingly connected world to save more lives, so that no patient is left behind.

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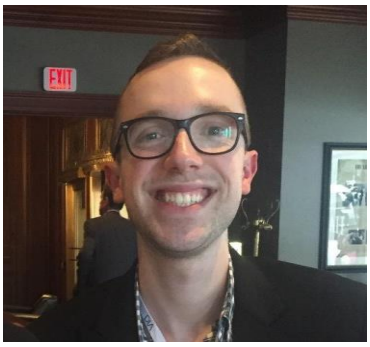

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THE LEGAL LANDSCAPE

Swimming with the Sharks—Best Practices in Informed Consent

Robert King

With more than a million lawyers working in the United States and a quarter million deaths caused by medical malpractice over the past decade, we are awash in litigation.

In assessing medical claims, an attorney will examine the ease of proving fault; the potential range of damages; and whether readily available funds exist, so that winning a case results in quick payment.

Generally, the plaintiff's lawyers are only compensated when they recover damages. For these lawyers, medical claims are a veritable cornucopia offering potentially huge damages, sympathetic clients who have suffered real trauma, and defendants who maintain robust insurance policies. Clinical trials, which are by their very nature experimental, can add deep-pocketed life science companies to the mix.

One of the best ways to ward off these claims is to have a professionally written and well-executed process for obtaining and preserving a subject's informed consent. Done properly, the informed consent makes it far more difficult to prove liability. As a result, a counsel faced with going up against a strong informed consent is less likely to accept the case. When a counsel does take on a client who is contesting what appears to be a nearly impregnable informed consent, he or she may moderate the reparations being demanded to reflect the heightened risk of losing in court.

What is Necessary for Effective Informed Consent?

Obtaining valid informed consent requires four things:

Capacity—The subject must have the legal and mental ability to make medical decisions.

Sufficient Information—The medical provider must disclose sufficient information regarding the diagnosis and proposed treatment of the medical condition, as well as have a discussion with the subject on potential alternatives. The provider must also detail the expected benefits and risks, as well as the likelihood that these benefits and risks arising from the various treatment options, so that the subject can make an informed choice regarding his or her own care.

Comprehension—The subject must indicate his or her understanding of the information provided.

Free Will—The subject must voluntarily grant consent without duress. This means that he or she cannot be coerced by anyone or by any aspect of the circumstances under which the informed consent was obtained. For example, obtaining consent immediately prior to a surgical procedure might open the consent to attack if the subject claimed he or she was under undue stress at the time.

If any of these components is weak or missing, then Christmas will come early at the Bar Association.

How Medical Providers Can Protect Informed Consent

When I was growing up in pre-internet Philadelphia, *The Daily News* had big headlines, short words, and the best sports section. It had a reputation for never using any word with more than three syllables (other than “interception” during football season). The paper’s style reflected its demographics—half the readership was working class and the other half was made up of professionals, so a happy middle ground of readability had to be struck.

Drafting an effective informed consent presents identical challenges. Complex information must be conveyed to a varied audience in a thorough, yet understandable manner. Present too much

technical information and comprehension fails. Or perhaps, the information will speak to subjects' fears because they misunderstand the probability of potential adverse events. Keep it too simple and the consent will fail because insufficient information was given.

The best approach is to provide the key information, but in a way that is as understandable to a layperson as possible. To accomplish this:

- Keep sentences and paragraphs short.
- Break sections up using clear headings.
- Avoid medical jargon.
- Emphasize the voluntary nature of the trial to reduce unjustified fears about trial risks.
- Proactively throughout the trial obtain feedback allowing concerns to be addressed.

One of the major obstacles to writing effective informed consents is that the legal and medical experts doing so are too familiar with the topic. To succeed, they must write the document so it can be understood by a merely average student at a mediocre junior high school.

The Devil is in the Details

Often, healthcare professionals treat the creation and management of informed consent documents as distasteful chores that need to be gotten through. Further, sloppy compliance with the technical requirements for execution regularly undermine what otherwise would have been effective documents.

Examples include:

- Relying on administrative personnel, instead of healthcare professionals such as a physician's assistant, to be present to witness the consent process and to ensure that all necessary information is provided.
- The principal investigator fails to countersign the document.
- The person obtaining the consent fails to properly capture the subject's signature and the date of when it was executed.

Technical errors such as these can loom large in court, so an effective system to ensure strict compliance with the key details of the consent process is paramount.

Google is My Lawyer

Informed consent agreements generated by counsel have been vetted by legal and compliance professionals, which can provide tremendous protection against successful lawsuits.

“Legalese” attaches tremendous importance to the use of particular words or phrases in very specific manners. A single word out of place can have catastrophic results. With so much at risk, cutting and pasting language from the internet into an informed consent is an easy shortcut, but one that can lead to expensive consequences.

The Simple Pleasure of a Nice Conversation

Never present the informed consent as “just” another document. Nothing will undermine confidence in an informed consent than simply handing the form to subjects and telling them to “sign it.”

The informed consent should be part of a give-and-take conversation. Glossing over risks or presenting trial details quickly can boomerang when subjects later claim they did not adequately understand the medical risks of the study they had joined. Having a real conversation regarding the benefits and risks of the trial also allows the medical team to assess a potential subject’s state of mind, encourages recruitment, and helps everyone spot problems before they occur.

The Dog Ate My Homework

Across America, the first sign of spring occurs with millions of people frantically searching for misplaced tax documents to prove their claimed expenses, deductions, and allowances. Clinical trials involving hundreds of subjects and thousands of pages of data are similarly complex, and an informed consent agreement—no matter how good the faith was upon its collection—will be of no assistance if it is lost and problems with the trial arise.

If you want to annoy a judge, few things will raise his or her blood pressure more than “spoilation of evidence.” Missing data and documentation can lead to significant sanctions by the court. Accordingly, preserving access to informed consents, whether digital or hardcopy, is vital.

Do Not Put Off Until April What Should Have Been Done in February

Like a teenager putting out the trash, distasteful chores tend to be put off until the last minute. Too often, developing a consent document that fits the characteristics of a particular trial happens too late.

The informed consent must pass muster with clinical teams, administrators, sponsors, and the institutional review board—all of which takes time. Ramping up at an earlier date drives better outcomes. By developing templates sooner, there is time to develop consensus while avoiding last-minute pressures.

Conclusion

Informed consents represent a vital protection for medical providers, but there is a tendency to treat them as just part of the "routine." Easily avoided errors result in devastating expenses because medical providers are much too busy to review their existing procedures. Taking a hard look at existing informed consent procedures in the near term is a far more cost-effective and pleasant choice than taking your chances once a lawsuit has been filed.

Robert King (Robert.King@tpclinical.com) is an attorney with more than 20 years of healthcare experience and founder of TakePoint Clinical, a firm whose credo is that "Medical Research is too Important to Wait on Endless Negotiations." A white paper providing step-by-step instructions on how to speed clinical negotiations is available for download at the firm's website (www.tpclinical.com).

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OVER THE TRANSOM

Stakeholders Aim for Success with Refined Patient Recruitment and Retention Tactics

Gary W. Cramer

As I write this, I have very recently observed my 15th anniversary of working for ACRP (gifts of crystal and ruby are appropriate, thank you very much), and while a lot of things about the clinical research enterprise have stayed more or less the same since my introduction to it, many other things have changed—mostly for the better. For example, as may be appreciated from the following snippets of content from a variety of sources (no endorsements implied), organizations still recognize the huge importance of effective patient recruitment and retention in the pursuit of drug and device development—only now, they are far more likely to be vocal about research ethics and the steps they have taken (or that should be taken) to make participation in studies easier and more rewarding for would-be volunteers.

You *Can* Get There from Here

Ride Health, a provider of transportation for patients in need, has partnered with the COVID-19 Prevention Trials Network of the National Institute for Allergy and Infectious Disease to ensure the network's vaccine trial participants can get to study sites when experiencing symptoms of COVID-19 after receiving a vaccine or placebo. Tracking and verifying COVID-19 infections among participants is crucial for obtaining enough data between vaccine and placebo arms to draw conclusions on safety and efficacy, making timely and safe transportation an important resource for study teams at more than 100 trial sites across the country currently testing the vaccines.

Study coordinators can request rides on behalf of participants within the Ride Health platform, where a native COVID-19 screening captures each participant's COVID-19 status. This screening is factored into the automated decision logic for trip assignments and ensures rides are fulfilled by individually vetted transportation providers equipped to meet driver and passenger safety standards. Once the platform schedules a trip, participants navigate rides via text message, automated phone call, or inbound phone system to ensure consistent access regardless of their comfort with technology.

Let's Talk Research Ethics

The exposure of research participants to the risk and burden of the research process must be justified, and research ethicists like Jen McCormick with the Penn State Clinical and Translational Science Institute study the balancing of research principles. The following commentary by McCormick comes from a recent podcast aimed at helping listeners learn about the research process and the benefits of health research conducted at institutions such as academic medical centers to their local communities.

Research ethics is conducting research in an ethically and socially responsible way. Research ethics can be referred to as responsible conduct of research, but ethical research actually takes it one step further than responsible conduct. Responsible conduct of research is following the rules and the regulations—which is very important, and that's part of ethics—but ethical research is taking a step beyond that and thinking about how the research fits into social values.

…[Y]ou have to think about who benefits? Is there any social good that can come out of this? And in particular, when humans are participating in the research, are people adequately informed? There's an element of what's right and wrong, but there is a huge gray area.

Personal health information, medical record information, genomic information, and public perceptions around those are some things that I am personally interested in. It's a really important ethical issue to make certain that researchers are using appropriate mechanisms to access and use that information, and to determine whether they're able to share it or not share it. I'm really interested in this idea of data sharing and data use and access. When people are participating in research, a lot of times, researchers want to share that information broadly. So,

it's really important to have language within the consent document that reflects that these data will be shared broadly.

…Another thing I can think about is the return of research results—whether a research finding should be returned to a participant or whether it's still too much research and doesn't have clinical utility or usefulness. And if that research finding should be returned, I can help the investigator think about how it should be returned.

Elevating Access to an Art

The MMS Holdings contract research organization has joined a historic alliance of 50 life sciences and healthcare organizations that seeks to accelerate the broad adoption of patient-focused, decentralized clinical trials and research. The Decentralized Trials & Research Alliance (DTRA), which launched in late 2020, plans to unite industry stakeholders, including healthcare companies, regulators, patient groups, and research organizations with a singular mission to make clinical trial participation widely accessible by advancing policies, research practices, and new technologies in decentralized clinical research.

"We believe that innovation and growth has a place in every part of our industry, and the proliferation of decentralized clinical trials is set to become one of the biggest changes that we've seen in industry in the past decade," said Eric Harvey, director of biostatistics and data science for MMS.

Decentralized, Not Dehumanized

THREAD, a technology and service provider that enables decentralized clinical trials (DCTs), and 1nHealth, a digital technology company that works with study sponsors on patient recruitment goals, have formed a new strategic partnership to enhance recruitment and retention outcomes in DCTs. According to the companies, the partnership integrates THREAD's globally leveraged DCT platform with 1nHealth's global digital recruitment solution to provide research organizations a differentiated approach to implementing scalable, best-practice digital recruitment for DCTs. The platforms are said to work together to reduce startup timelines, increase enrollment effectiveness, and ensure participant satisfaction.

"DCT approaches are enabling sponsors and [contract research organizations] to reach a larger and more inclusive participant population. To successfully engage this broader population, an innovative, remote approach that reduces participant and site friction is necessary," said Joss Warren, director of partnerships at THREAD.

Dispensing with Disparities in Designing Medicines

In a perspective piece published in the February 5 issue of *Science*, pharmacologist Namandie Bumpus, PhD—who recently became the first African American woman to head a Johns Hopkins University School of Medicine department, and is the only African American woman leading a pharmacology department in the country—outlines the molecular origins for differences in how well certain drugs work among distinct populations. She also lays out a four-part plan to improve the equity of drug development.

Genetic variants can be more likely to occur in some ethnic groups versus others, and, as a champion for diversity in science, Bumpus advocates that these differences make it even more important to increase diversity in clinical trials of new drugs and therapies. Yet, many clinical trials continue without diverse participation, potentially leading to poor outcomes for people of color and less access to emerging therapies.

Now, as new treatments and vaccines sweep us toward a critical turning point in a pandemic that has disproportionately affected people of color, the need for better standards for diversity in clinical trials is greater than ever, says Bumpus. However, simply increasing the number of underrepresented minorities in clinical trials is not enough to solve the systemic problems, she adds.

Bumpus' framework for better drug development includes a four-part plan involving the laboratory research of cellular and animal models to study genetic variability; better hiring practices to diversify the scientific workforce; diversity requirements for funding agencies; and diversity reporting requirements on clinical trial demographics in articles published in scientific journals. She says the framework may compel the drug development field to take steps toward a future where "treatments are most likely to work for all people" and "existing health disparities are not further exacerbated."

Gary W. Cramer (gcramer@acrpnet.org) is Managing Editor for ACRP.