Clinical Researcher

The Authority in Ethical, Responsible Clinical Research

October 2024 (Volume 38, Issue 5)

Always be Curious, Never Stop Learning

Clinical Researcher

Association of Clinical Research Professionals

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As project scopes and protocol complexities continue to grow, trial-related technologies emerge and mature, and new areas of specialization in the clinical research enterprise drive workforce evolution, contributors to this issue invite you to study the theme of "Always be Curious, Never Stop Learning"—focusing on critical facets of ongoing education, training, and research regulation and management so that you can stay ahead of the curve in an ever-changing environment for drug and device development.

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CHAIR'S MESSAGE

Celebrating a Season of Success

Elisa Cascade, MBA, 2024 Chair of the Association Board of Trustees for ACRP

It's October! The weather is getting cooler, the leaves are changing, candy is everywhere, and my boy's favorite cereal, Count Chocula, is now in the grocery stores again.

October is also the time for the 2024 ACRP/Academy Membership Meeting, and there is so much to celebrate this year! During the virtual meeting earlier this month, we discussed how ACRP is advancing the people and practice of clinical research by:

- Being the most passionate advocate for you—ACRP is leading the charge for recognition of clinical research as a profession in the Occupation Codes maintained by the U.S. Bureau of Labor Statistics and reviewed every 10 years.
- Providing the tools you need for career success—In the last year, more than 23,000 clinical research professionals participated in ACRP training and continuing education programs.
- Creating connections through Community—ACRP now represents a growing global community of more than 17,000 members in 73 countries.
- Giving employers the confidence to know their teams are the best of the best—ACRP is working with more than 40 organization members whose leaders understand and value the significant contributions that our more than 40,000 certified clinical research professionals bring to high-quality trial conduct.

- Leading the way for Workforce Development—There is growing demand for a diverse, research-ready workforce, and ACRP itself is driving new talent into the industry through educational grants and scholarship programs. Quick shout-out and a big thank you to Sergio, Rick, Scott, David, Kyle, Lauren, and Justin—the riders who recently raised nearly $85,000 through the Ride4DEI's fourth annual bicycle trek in support of our workforce.

Lastly, October marks Breast Cancer Awareness Month. It's hard to imagine anyone out there who doesn't have a colleague, friend, or family member who has been diagnosed with the disease. To all of you, we wish you strength and courage in your fight, and the hope that one day we will find a cure to end breast cancer.

—ACRP—

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PEER REVIEWED

Optimizing Clinical Trial Education in Academia

Tony Succar, PhD, MScMed(OphthSc); Araksi Terteryan, MPH; Karen Manrique, MS; Eunjoo Pacifici, PhD, PharmD

Clinical trial education is the key to optimizing quality in trials, developing investigational medical products, and improving patient healthcare outcomes globally. Clinical trials are considered the gold standard for evaluating investigational medical products as safety, efficacy, quality, and regulatory approvals are based on scientific evidence. Similarly, the subjects covered (and how they should be presented) in clinical trial education should be evidence-based, rather than being left to the personal judgments of instructors, tradition, or other biases.

Clinical trials are becoming more complex in design and continue to evolve due to emerging treatments such as regenerative medicines utilizing innovative gene and cell therapies for conditions which were long thought of as incurable. Furthermore, greater-than-minimal-risk clinical trials investigating novel and invasive treatments can result in serious adverse events leading to hospitalization and death. Thus, formal competency-based education is crucial in replacing traditional on-the-job training.

To optimize clinical trial education, key areas of clinical and translational research must be implemented to produce graduates who demonstrate core competencies in the design, conduct, analysis, and monitoring of clinical trials. This paper highlights educational strategies for teaching clinical trials and serves as a basis for future research regarding the development, implementation, and evaluation of clinical trial education.

Background

Tremendous advances in science and medicine have been made as clinical trial design and quality have improved over the years, leading to enhanced validity, efficiency, and reporting. Clinical trials are crucial for developing new medical interventions and improving the quality of patient care worldwide. As the ultimate goal is to gain regulatory approval, optimizing clinical trial education will produce competent clinical trialists for the design, ethical conduct, monitoring, and analysis and dissemination of trial data, ensuring compliance with local laws and regulations.

Education also improves public awareness, recruitment, and retention of participants, which are all crucial elements to the success of trials. Just as clinical trialists base the safety and efficacy of investigational products on scientific evidence, educationalists must similarly base their teaching practices on sound educational evidence and theory.

In line with this, the Joint Task Force for Clinical Trial Competency (JTF) has developed a framework that outlines the core competencies for clinical research professionals, as described next (Sonstein and Jones, 2018).

Clinical Trial Competencies

The eight core competency domains for clinical research professionals developed by the JTF include:

1. *Scientific Concepts and Research Design*
2. *Ethical and Participant Safety Considerations*
3. *Investigational Products Development and Regulation*
4. *Clinical Study Operations (Good Clinical Practice [GCP])*
5. *Study and Site Management*
6. *Data Management and Informatics*
7. *Leadership and Professionalism*
8. *Communication and Teamwork*

The purpose of this framework is to provide a standardized set of competencies for clinical research professionals to facilitate consistent education, training, and professional development. The framework bolsters workforce development efforts by defining the essential skills and knowledge required for various roles in clinical research. This is important, as the competencies guide the design and evaluation of academic programs and training curricula to ensure alignment with industry needs and accreditation standards, and aid in the development of performance evaluations and career advancement pathways for clinical research professionals. Thus, these competencies are used to formalize education in clinical research and, due to the evolving clinical trial landscape, they should be maintained through continuing education initiatives.

Based on this framework, the Association of Clinical Research Professionals (ACRP) developed a Core Competency Framework for Clinical Study Monitoring™, which outlines the core competencies required for individuals involved in clinical study monitoring.

With some editing for clarification, the following list covers the first-ever set of monitoring competencies harmonized with the Core Competency Framework for Clinical Research Professionals developed by the JTF. A monitor should possess an understanding of:

- *Subject confidentiality and data rights and privacy*
- *The product development lifecycle and significance of design features in clinical trial protocols*
- *The informed consent process*
- *Subject recruitment and retention at the investigator site*
- *The identification, reporting, and resolution of suspected misconduct*
- *Compliance (including any amendments) to ensure protection of the rights and well-being of patients and the integrity of the study and data*
- *The International Council for Harmonization (ICH) tenets for GCP*
- *Adequacy of approvals or notifications to ethics committees/institutional review boards (ECs/IRBs) and/or regulatory authorities*
- *Identification of differing safety events and understanding the reporting requirements of each*
- *Training compliance*
- *The purpose of essential documents and the requirements for maintenance and archiving*
- *Audit and inspection processes*
- *The roles and responsibilities of, and relationships between, the clinical research associate and investigators, sponsors, and ECs/IRBs per ICH GCP*

- *The requirements for accurate and complete site source documents (verification that data reported in the case report form are consistent with source documentation)*
- *How to plan and conduct all types of monitoring visits*
- *Time management and prioritization of work*
- *How to verify that biosamples have been appropriately handled, stored, labelled, and shipped*
- *How to verify that third-party vendor data are appropriately collected, transferred, and stored*
- *Investigational product (IP) accountability, the IP chain, and IP blinding*
- *Assessment of principal investigator qualifications and resources*
- *Critical data and processes*
- *Query issuance and resolution*
- *Clinical trial systems of record*
- *Compliance with electronic record requirements and regulations*
- *Personal work product accountability*
- *Cultural awareness and sensitivity*
- *Professional behavior*
- *Their relationship and communication with clinical study team members and investigative site staff*

Additionally, ACRP has developed Core Competency Guidelines for Clinical Research Coordinators™.

Global Clinical Trial Educational Strategies

With clinical trial registries showing increasing trends in the number of trials being conducted globally, educational programs are needed to meet a growing demand for trained professionals. Moreover, education should be more formalized to provide sustainable careers.

In some cases, educational programs for clinical research professionals are degree-conferring programs focusing on clinical trial management. In other cases, organizations have developed self-study modules, self-help web portals, and symposia that are freely accessible to help address constraints of budget and resources in an academic environment (Manrique et al., 2024) (see Table 1). Although quality investigator-initiated trials play a crucial role in product development, gaps still exist in training the professionals to conduct clinical trials properly (Spinrad et al., 2019). This has provided an impetus for academic and non-academic institutions to develop various educational and training programs and tools.

Table 1: Educational Training for Clinical Research Professionals*

Resource	Description	Target Audience	Mode	Link
Regulatory Resource Web Portal	Overview of regulatory information and resources to guide clinical research professionals in their approach to planning and conducting clinical trials in the U.S.	Clinical Research Professionals, Academia	Online, Self-Help	https://sc-ctsi.org/resources/regulatory-resources
Online Study Modules	Free self-study modules providing fundamental and practical knowledge of clinical research monitoring, auditing, and U.S. Food and Drug Administration site visit readiness, with an emphasis on investigator-initiated trials.	Clinical Research Professionals, Academia	Online, Self-Paced	https://uscregsci.remote-learner.net/login/index.php
Regulatory Science Symposia	Educational symposia focused on various subjects relevant to current needs and requests of the clinical trial workforce.	Clinical Research Professionals, Academia, Industry	Live Symposia	https://mann.usc.edu/departments/regulatory-quality-science-department/dk-kim-center/capacity-building/regulatory-science-bootcamps-symposia/

Resource	Description	Target Audience	Mode	Link
Translational Workforce Development Online Training Catalog	Online training catalog focused on subjects relevant to current needs and requests of the clinical trial workforce; Expanding broad availability of symposia material.	Clinical Research Professionals, Academia	Online, Self-Paced	https://twd.ce.emorynursingexperience.com/

**This work was supported by grant UL1TR001855 from the National Center for Advancing Translational Science of the U.S. National Institutes of Health (NIH).*

There is an emerging need for more academically inclined and structured education for clinical research professionals to prepare them to handle the rising complexities of conducting and managing clinical trials. However, most industry employers focus on in-house training basic concepts, assuming that the employees will learn the rest through experience. This on-the-job training, however, may be narrow in scope and not provide trainees with the ability to see the complete lifecycle of medical product development and respond to unexpected occurrences. The additional time and resources dedicated to training clinical researchers with no formal qualifications could better be spent on high-level tasks of conducting clinical research.

The NIH and ACRP offer educational resources and programs on clinical trials. Further educational strategies which have been implemented in clinical trial curricula include a study in Australia describing the use of a simulation workshop in teaching the clinical research process to nursing students. This study demonstrated an increase in both students' interest and knowledge (Lee and Peacock, 2020). Burhansstipanow and colleagues developed a clinical trials curriculum

for Native Americans and outlined their lessons learned from this curriculum (Burhansstipanow et al., 2003).

Moreover, Yan and colleagues described in detail a simulation-based clinical research curriculum developed in China. The curriculum was divided into the design and implementation stages of clinical trials and observational studies, containing 16 classes. Students were engaged in simulation as an investigator, as well as experiencing a variety of simulation role changes, including for statisticians, sponsors, monitors, and ethics committee members. The simulation content covered protocol writing, review and approval of clinical trials, registration, and implementation of randomization, masking, and statistical analysis. Oral reports and record files were used for the formative evaluation of each simulation, which included debriefing with guided reflection questions (Yan et al., 2022).

The University of Hawai'i Cancer Center implemented a clinical trial education intervention for medical students, including lectures, resource manuals, problem-based learning scenarios, and optional practicums. After completing this comprehensive intervention, there were significant increases in students' understanding, knowledge, and positive attitudes toward clinical trials. (Anzai et al., 2023). Exposure to clinical trial education during medical school can influence future practice patterns and increase patient referrals to clinical trials (Anzai et al., 2023).

Early simulation in research teaching were conducted by Peacock (Peacock, 1981) and Thiel (Theil, 1987) and high-fidelity simulation in clinical research training was first reported in 2004 (Taekman et al., 2004), which used a patient as a simulated study participant and found the simulation exercise could increase their confidence in developing a clinical research protocol. For simulation teaching in specific research design, an outbreak investigation simulation was developed to teach nursing students principles of epidemiology (Okatch, 2016). A study conducted in Korea reported on the feasibility and positive effects of a simulated clinical crossover trial to teach clinical studies, during which students were randomly grouped to distinguish between two different types of cola as simulated subjects (Kim et al., 2020).

Potential benefits of the incorporation of simulation into clinical research were reported as including decreasing the learning curve for protocols, improving study design, and increasing

participant safety (Brindley et al., 2009). Other advantages of simulation in clinical research education include enhancements to practice and engagement, interactivity, teamwork training, case-based coherence, professionalism, and student-centered active learning, and the use of comprehensive ability exercises allowing students to make mistakes in a safe environment (Yan et al., 2022). This last study also noted that the challenges for simulation include significant effort expenditure by students and teachers, insufficient faculty specializing in both clinical research and simulation teaching, dependency on well-designed cases/scrips, requirements for certain environments and equipment, and the fact that this approach is not applicable for large classes.

Conclusion

Clinical trial education in academia is crucial for fostering greater appreciation and patient engagement in clinical research, ultimately contributing to the advancement of medical knowledge and improved healthcare outcomes. In addition, clinical trial training and education need to be more formalized through university postgraduate education to provide a sustainable workforce.

The competency framework developed by the JTF and ACRP serve as valuable resources for academic institutions, employers, and professionals in the clinical research field, promoting standardization, quality, and continuous improvement in the conduct and monitoring of clinical trials. The competencies provide a standardized approach to clinical research education and professional development, ensuring that research professionals across different roles and regions have a common understanding of the essential skills and knowledge required in clinical research. These competencies, as well as the development of longitudinal assessment strategies, need to be implemented to ensure that their goals are met and that the education is evidence-based.

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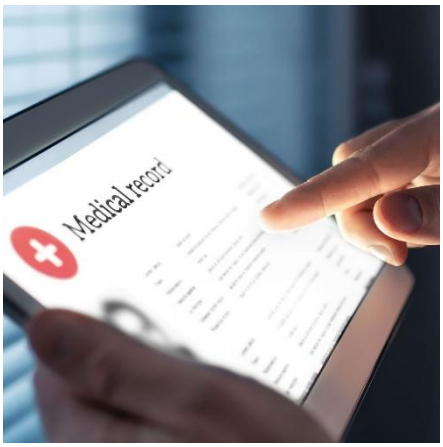
PEER REVIEWED

A Case Study on Training Initiatives to Support Clinical Researchers with Electronic Medical Records

Paula Smailes, DNP, RN, CCRP; Courtney Gillespie Saslaw, MLT



Informatics competencies are important for all clinical research professionals. In 2014, the Joint Task Force for Clinical Trial Competency identified eight essential competencies, with data management and informatics identified as crucial skills for the clinical research workforce.{1} Using new technology and data sources for clinical research studies is now a normal expectation of clinical research data management.{2} When research staff are competent in their roles, the quality of their work is enhanced. With numerous information systems being necessary to execute a clinical study, what is the best way to train our research workforce? This case study provides an overview of an electronic medical record (EMR) training conversion from instructor-led to eLearning for clinical researchers at our academic medical center (AMC), and further elaborates on training initiatives after onboarding to support competency.

Clinical Research and Electronic Medical Records

Clinical researchers with a full or partial waiver of the Health Insurance Portability and Accountability Act (HIPAA) Privacy Law for their protocol may access our EMR system. Access provisioning follows the minimum necessary rule of HIPAA, which states that covered entities may only access, transmit, or handle the minimum amount of private health information needed to complete a specific task.{3} For this reason, researchers are provisioned access to only the workflows they need in our system.

Our AMC has close to 6,000 clinical research studies in its EMR system and examples of clinical research workflows for which EMRs may be useful include such tasks as recruitment, data mining, source documentation, reporting, and research billing charge review. Data from EMRs can also promote research with information related to the effectiveness of drugs and therapeutic interventions.{4}

Key to access provisioning is training. More than 300 newly hired clinical researchers take our clinical research EMR training each year from many possible curriculums. The type of training taken matches the type of research access needed. Positive outcomes have been found from EMR training, the most common being change of learner knowledge and skills.{5} It is a policy at our organization that EMR training must occur prior to system access.

When our organization first went live with its EMR system, instructor-led training took place in a computer lab with each end user at a computer working through tasks. However, the push for healthcare organizations to convert to EMRs became the stimulus for our organization to change how we deliver our EMR training. As an increased number of onboarding staff arrived at our organization with prior experience with our Epic-based system, we began to rethink how we could capitalize on that existing end-user knowledge.

Our high-volume roles like nurses and providers were converted first, starting in 2015, and slowly over time other roles made the same conversion. By 2020, our clinical research curriculums began their conversion to eLearning with the onset of the COVID-19 pandemic giving an additional push for remote onboarding.

eLearning

The conversion to eLearning is advantageous for both end-users and our training team. The benefits for end-users are that it becomes a means for training that can be taken any time, any place, and at the users' own pace. It also serves as a source for refresher training with the same convenience. For the training team, it frees up time that would otherwise be used for classroom instruction to focus on optimization efforts. Additionally, training can be standardized within a single eLearning product, whereas in-person training across several different trainers cannot.

However, eLearning is a time-consuming process for development. There is a multi-step process (see Figure 1) that involves several team members (see Table 1) to ensure both quality and meaningful content are maintained as the development flows to completion.

Figure 1: eLearning Conversion Process

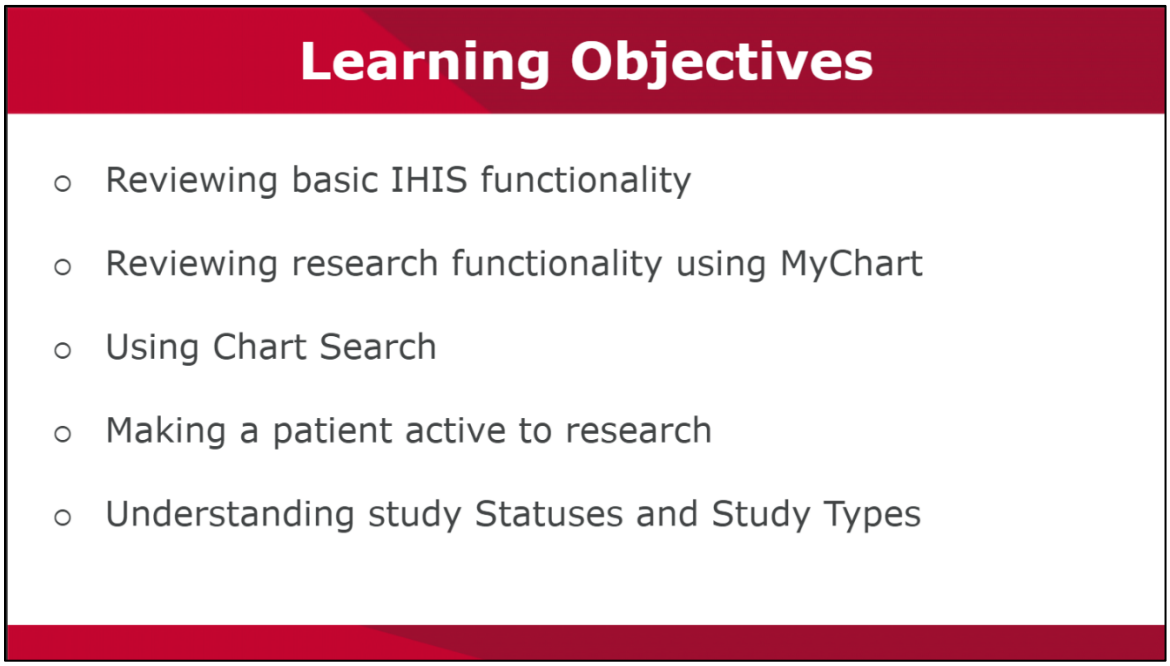
Table 1: Roles Needed for eLearning Development

Role	Description
Principal Trainer	A content expert for workflow who assures that materials are current.
Instructional Designer	An eLearning development expert who assists in making the eLearning effective and compliant with established organizational templates and standards.
Technical Editor	This role is essential for the quality assurance process in terms of reviewing content for spelling and grammar.
eLearning Developer	Works to create the Storyboard, Captivate, and Storyline files (Adobe products) using the AMC's style guide and eLearning principles established by the instructional designer(s).
Subject Matter Expert	An additional team member, such as a builder or someone in a leadership role, who knows workflows and targets end-users who can provide additional insight for development.

Development Process

One of the first steps in eLearning conversion is the development of a design document. The principal trainer for clinical research and instructional designer at an organization should meet to discuss the lesson plan used for instructor-led sessions and determine the breakdown of the curriculum into courses and lessons. Objectives for each lesson are determined which help to drive the content (see Figure 2). Powtoon videos can also be developed, though these are typically better for content-heavy lessons versus workflow-related training. The design document is created in Excel and shows the development timeline from start to finish, as well as the progress made toward each milestone.

Figure 2: Example eLearning Objectives for Research Curriculum



Essential to the early phases of development are ensuring that the existing lesson plans and exercise workbooks are current, as well as compliance with our eLearning style guide. Given an EMR system that changes quarterly, oftentimes changes are impactful. These lesson plans serve to guide eLearning content.

Once lesson plans are ready, a Storyboard is created from them. A Storyboard is a vision board that takes the lesson plan content and places it in a PowerPoint document. Key to this phase is using the necessary templates and language, which provide standardization across multiple curriculums and clinical roles. The Storyboard includes step-by-step screenshots of workflow through which the researcher will ultimately progress.

Essential to Storyboard development is creating scenarios that are engaging and realistic. The importance of racial, gender, and age diversity should not be overlooked when stock pictures of people are included to represent patients and clinical research workers to establish clinical research scenarios.

Once the Storyboard has gone through quality assurance, it is placed in Adobe Captivate. This takes the non-interactive Storyboard and makes it into an interactive simulation. For example, if the directive is “click here,” Captivate will progress to the next slide after the researcher clicks in the designated spot, thus creating the simulation. Upon completion, the Captivate file will go through quality checks to make sure the timing and functionality are working appropriately.

While the Captivate file is being developed, the principal trainer for clinical research can be creating assessment questions. These questions quiz the researcher on content taken. The assessment questions go into a template, then through the quality assurance process to ensure standardization in verbiage, such as whether or not the questions match the objectives of the course. Assessment best practices, such as avoiding “All of the above” or “None of the above” as answer options should be considered. Ideally, having accompanying screenshots with the assessment questions can help the learner answer appropriately.

Deployment

When the assessment questions and Captivate file are complete, they are packaged and placed into Storyline. Our AMC’s organizational branding is included, then it is loaded into our learning management system (LMS) for a pilot run (see Figure 3). This ensures that the lessons within the course launch successfully, that assessment questions advance appropriately for correct and incorrect answers, and that the course objectives are included. Ultimately, this testing helps us to

ensure that the course lands on the completed transcript if passing the assessment, while failed assessments should remain on the active transcript.

Figure 3: Example of Research Course in LMS with Organizational Branding

Once ready, the official launch of the eLearning is made in our live LMS. Occasionally issues arise once the training is live, such as screens that fail to advance when prompted. Resolution of these issues occurs from our eLearning team. Lesson plans are created from the Captivate files after deployment and will be used for future maintenance. Maintenance occurs every two to three years, whereby the development process is repeated except there is no Storyboard. The screenshots are updated and placed into Captivate with updates to workflows and verbiage as needed. If a major system change occurs, then a request could be made to the eLearning team prior to the standard maintenance schedule.

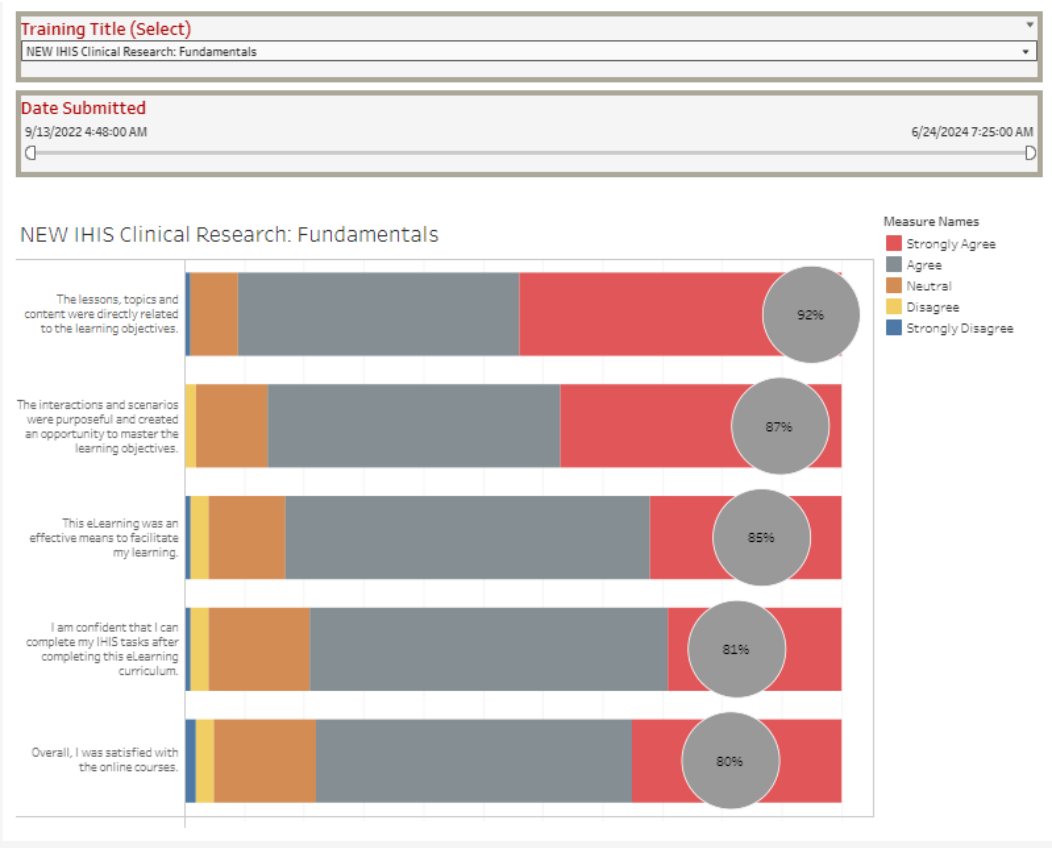
eLearning Satisfaction Survey

At the conclusion of each eLearning is an eLearning Satisfaction Survey. This provides the researcher an opportunity to give feedback on this method of training. The survey consists of five questions in a Likert scale format. The survey is not a requirement and will automatically remove itself from the transcript after two weeks.

One example of an eLearning Satisfaction Survey is from our Clinical Research Fundamentals course. Results show that over a 21-month time frame, most of the 110 researchers who

completed the survey found the content favorable (see Figure 4). Feedback for all research curricula is monitored on a continued basis and considered when courses go to maintenance for improvement opportunities.

Figure 4: eLearning Satisfaction Results from Clinical Research Fundamentals



Initiatives After Initial Training

When a newly hired researcher is onboarded, there may be a time gap between initial EMR training and access provisioning. As more time passes, there is an increased likelihood that learned content will be forgotten. For this reason, it is important to make sure that training is taken as close to access provisioning as possible. The forgetting curve is well known, and evidence has suggested memory phases that reflect time frames of memory decline.{6} As previously mentioned, one of the benefits of eLearning is that it is a 24/7 source for refresher training, should the researcher need it.

Competency Checklist

One useful tool that can be used by management is the Competency Checklist. This checklist, created per the EMR training course, serves as a guide to determine if the researcher can show mastery of system functionality. When deficits are found, they can be learning opportunities to address with the lead trainer, educator, preceptor, or leadership to help bridge knowledge gaps.

Onboarding Sessions

Onboarding sessions are opportunities to spend 1:1 time with the principal trainer of clinical research at our AMC. These 30-minute sessions review learned content from the eLearning, but applied to the researcher's therapeutic area. The time is spent creating study reports and doing system customization to help them find information quickly and document efficiently. These catered sessions are completed virtually to allow for higher productivity for the trainer by eliminating travel time. Researchers across our enterprise could be up to 20 miles apart, and the virtual option allows for more time onboarding instead of traveling.

Sessions are conducted using Microsoft Teams with screen sharing, which allow for system guidance, just as if sessions were conducted in person. A report is completed by the trainer on covered topics, and this can be shared with the new hire's manager. At the conclusion of onboarding sessions, researchers are sent an email with important tools and workflows that were covered during the session.

Rounding

Rounding is an initiative that is part of ongoing optimization for researchers. As previously mentioned, our research end-users are geographically dispersed across our county. Rounding is an opportunity to meet the end-users at their location and address any system issues at a time that is convenient for them. Rounding may consist of targeted topics or address the latest system changes. A report can be done per division and shared with leadership, but can also be used as a tool to track common trends.

Training Materials

A variety of tools are used to help research end-users with workflows. Tipsheets and Quick Start Guides are condensed workflows in PDF format that can be sent to end-users when questions arise; they are targeted to specific workflows. Exercise books can be used to reinforce eLearning by providing scenarios to practice in a play environment. The resources, while helpful to end-users, must be kept current in the presence of constant system change.

Conclusion

It is important that new hires feel supported as they begin their research careers. The onboarding process can be a crucial time to help them transition to the organization and to develop knowledge about clinical research workflows and organizational policies. Including technology training, specifically on the EMR system, is at the core of clinical research execution at our organization.

The development of quality training initiatives can produce knowledge on efficient use of the system that ultimately can improve the quality of data and study productivity. While eLearning offers the benefit of convenience and easy access to refresher training, it should be noted that the development process is time consuming and involves many people to ensure the delivery of a quality training product.

Constant EMR system change means that training done as a new hire will no longer be effective in future years. Because of this, continued training initiatives must be done as a means of ongoing support, which ultimately leads to research study success.

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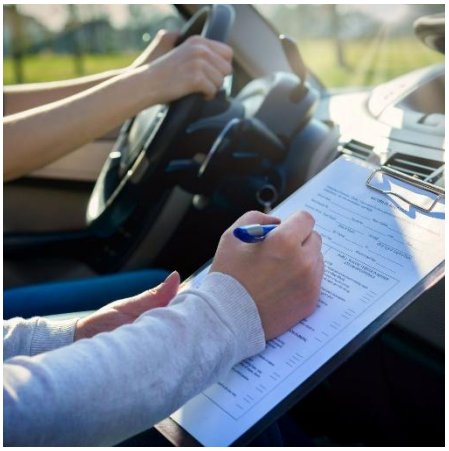
ON THE JOB

Back to Basics with Research Education

John R. Nocero, PhD; Andrea L. Bordonaro, MAT



Research managers know how important research education is, but it's easy to lose focus on workforce development goals at a study site when enrollment is down, protocol deviations are up, queries are unresolved, and monitors are breathing down your neck. It's funny—conducting clinical research in today's environment is like learning to drive, except that you don't learn by maneuvering your dad's Oldsmobile Cutlass through pre-arranged orange cones with a calm and supportive instructor belted in next to you. You gain your experience alone at night, careening through the snow on an icy bridge.

Managers today want new employees to come in and hit the ground running, but you need to spend time up front with these individuals—whether they are research-naïve newbies or seasoned veterans—to get a return on your investment in them. That means defining a full research training and development program tailored to your site to ensure all employees are appropriately trained on applicable regulations, guidelines, policies, standard operating procedures (SOPs), and study-specific tasks.

What's more, the necessary effort doesn't stop at onboarding. There needs to be a continuing education component, too—one building upon an employee's skills to keep them learning and growing.

A complete and robust research education and training program includes onboarding, a plan for an employee's first 90 days, and resources for continuing education as they progress at your company. Here's how to build one.

Onboarding

Your company should require all employees to go through a new hire orientation process, which should be facilitated in some combination by Human Resources, the Quality Department, and Training and Education. There are some basic components that this process should cover, from both employee conduct and organizational administrative perspectives.

Research conduct should cover a high-level overview of clinical research at the site, including workflow from study-start-up to closeout; a review of Good Documentation Practice (GDP), including an overview of the ALCOA+ principles for data integrity; and the International Council for Harmonization's tenets for Good Clinical Practice (GCP) (soon to be updated). An overview of the Collaborative Institutional Training Initiative (CITI Program) training on research, ethics, compliance, and safety and a high-level review of the site's quality management systems and other administrative materials should also be covered.

This is a difference from many onboarding programs currently in place focusing on a review of the company history and signing off on the employee handbook. Yes, those are important, but if managers have the expectation that employees are ready once they get to the site, onboarding training needs to be set up to align with role-specific training.

Role-Specific Training

A training matrix should be used to determine the training materials new hires must complete. These may come in the form of SOPs, work instructions, or user guides. The focus here goes from "Did they read our SOPs?" to "Do they understand our SOPs and can they carry them out as directed?"

There is the standard fare here that we are sure a lot of you already do do—review of the regulatory logs and protocols, for example, or obtaining life support certifications that you put in the study binder. However, these are not the items that cause sites to get an FDA Form 483 from the U.S. Food and Drug Administration; what does is not protecting participant safety or data integrity.

Reinforce the workflow of the clinical research process among your staff, stressing attention to GCP, GDP, and the ALCOA+ principles to reconnect new hires back to the priorities for participant safety and data integrity. It's why we are here. So that's where your focus should be, but you have to reinforce the lessons learned in onboarding.

Ensure the new employee has a preceptor to help them during protocol reviews and who can sit in with them while they conduct their first informed consent interview, enter data into the data capture system, or build the regulatory binder. A preceptor is an individual with demonstrated competence in a specific area who guides, assesses, and validates the knowledge, skills, and attitudes needed to transition to a new role, specialty, or environment in the healthcare setting. Preceptors are integral to the orientation and onboarding of new staff and staff transitioning to a new role or department, as well as for students' clinical experiences.

It doesn't matter how many years of experience their resume says they have. Going back to the driving analogy—all employees will perform to the basic level of their training. And if this basic level of training comes from another company, they don't know how to do things YOUR way; they are performing the way another company taught them.

Develop the competencies that cover the areas in which you need your employees to demonstrate knowledge. Write it all out and document it. But you are still not done. You need to have a plan for ongoing education.

Ongoing Education

Managers—how often have you tried to get rid of an underperforming employee only for Human Resources to ask you for documentation on their declining performance that you don't have? How often have you later regretted giving someone a "Meets Expectations" on their last evaluation, knowing they didn't really deserve it? Flip this script. Have weekly ongoing discussions with your employees. Find out where their educational gaps are and then give them resources—either internally within your Quality Department or externally from sources such as the Association of Clinical Research Professionals and Save Our Sites. Development of your employees is your responsibility. Invest in them for your organization's future.

At a minimum, all research staff should complete biannual training on GCP and GDP, with clinical staff completing Advanced Cardiovascular Life Support or Basic Life Support training as needed to maintain their certification.

Conclusion

We are not telling you anything you don't already know. But we are reinforcing that a focus on the basics is needed and can work. Rather than be triggered by the latest hack, weave the basics above into your work and nurture them throughout your employee's professional careers.


John R. Nocero, PhD, and **Andrea L. Bordonaro, MAT,** blog on LinkedIn as "The Q-Kids," discussing everything related to clinical research education, inspiration, and professional connection.

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RULES & REGULATIONS

The FDA's Final DCT Guidance—Agency Now Serving Up Decentralized Elements À La Carte for Fit-for-Purpose Trials

Pamela Tenaerts, MD

One of the first things that struck me about the U.S. Food and Drug Administration's (FDA's) newly finalized guidance on decentralized clinical trials (DCTs) was the title: "Conducting Clinical Trials with Decentralized Elements."

Historically, the clinical research industry has referred to a decentralized model as a DCT or hybrid trial. Now, the FDA is reframing it to simply be what it is—a clinical trial with decentralized elements, such as telehealth visits, electronic informed consent, and digital health technologies (i.e., wearable devices).

In this linguistic edit, the FDA has done two important things. First, the agency has made it clear that a clinical trial is a clinical trial and, as such, subject to all applicable laws and regulations regardless of how it is designed or what technology tools are leveraged. Second, the FDA has emphasized one of the greatest advantages of a decentralized model: Flexibility, in that trial sponsors can pick and choose decentralized elements á la carte style, so trials are designed to be fit-for-purpose, fit for the patient population.

Here's a look at additional changes for the better.

Data Oversight: Minimizing Data Variability

To account for multiple sources of data collection (via the site, provider, home health visit, sensors), the guidance suggests a data flow diagram should be available to show:

- Data origin
- Data flow
- Data transfer pathways
- Methods and technologies used, including service providers for data collection, handling, and management
- Transmission of reports

Study records should capture the visit type (i.e., telehealth or in person); the visit location (i.e., participant's home, local health care facility, traditional clinical trial site); the date of the visit; and the data originator.

PI Oversight: A Bit More Clarified, But Questions Remain

Clinical trial investigators should evaluate reports from local healthcare providers (HCPs) for abnormal signs or symptoms detected at in-person visits and follow up with participants as appropriate. Televisits can be used for principal investigator (PI) to supervise trial personnel, and the FDA no longer requires an HCP log compared to the draft guidance, but just names and dates of contacts need to be in records. PIs will need to review HCP reports for trial data quality, and questions remain how this will be operationalized.

Clinical Trial Visits

Remote visits can include telehealth visits, participant visits to local HCPs, or in-person visits by trial personnel or local HCPs to participants' homes. The schedule of events should clearly indicate which visits will always be at the site and which will be remote (the latter can be left up to the participants' choice). The trial team must address privacy for in-home assessments, whether telehealth or in person.

In addition, data collection can be done by nearby HCPs and ideally by a participant's treating physicians, if they do not differ from those the HCPs are qualified to perform. Therefore, no detailed trial knowledge is required as activities are not considered critical and essential to the

trial. However, trial activities unique to the trial need to be performed by qualified personnel (PIs, sub-investigators, and other trial personnel) who are appropriately trained and well-versed on the protocol and investigator's brochure.

Informed Consent

The FDA guidance says that informed consent should not be done by local HCPs, as they are not required to have protocol knowledge or specific clinical trial training. The consent forms should indicate if HCPs will be used in a trial and what trial activities will be done where—for example, at the site, at the participants' homes, or elsewhere. Who will have access to the participants' personal health information will also need to be further specified.

Safety Monitoring

Generally, adverse events should be captured during scheduled visits with investigators or trial personnel. Local HCPs performing trial-related activities may become aware of a concerning sign, symptom, or clinical event. The safety monitoring plan should describe how local HCPs will be instructed to report such findings, as well as what information will be collected via a digital health technology, how it will be used and monitored, and actions trial participants or personnel should take in response to abnormal findings or electronic alerts. Trial participants should also be able to arrange for an unscheduled visit with trial personnel using telehealth or an in-person visit, as appropriate.

Electronic Systems

Electronic systems can be used to perform multiple functions to manage DCT operations, including:

- Managing electronic informed consent (e.g., maintaining approved versions of informed consent, documenting institutional review board approval, archiving signed forms
- Capturing and storing reports from remote trial personnel, local HCPs, and local clinical laboratory facilities
- Managing electronic case report forms (eCRFs)
- Scheduling trial visits and other trial activities
- Tracking IPs that are shipped directly to trial participants

- Syncing information recorded by digital health technologies
- Serving as communication tools between trial personnel and trial participants

In all cases, the FDA says training should be provided to sites and participants. Real-time videos and audio interactions are a live exchange of information between trial personnel and participants, but the FDA does not consider these systems to be electronic systems specific for clinical trial purposes, so they are not subject to 21 CFR Part 11 in the *Code of Federal Regulations* (but they may be subject to local telehealth laws).

The Perfect Menu for Flexible Trial Design

Building a fit-for-purpose trial should always be top priority, but in all the recent hype around the potential of digital technologies, researchers may not have always deployed technology in ways that benefitted the trial design or patients. In some cases, the industry deployed technology for technology's sake—experimenting with innovations in hopes of operational improvement. After all, this is an industry rooted in experimentation to find new cures. Now with emerging data on DCT impacts and the FDA's re-characterization, we can confidently return to trial design fundamentals but with the option to leverage modern technologies á la carte style if—and when—they benefit the trial.

No more fixed menus…being able to choose what is optimum for individual trials is the ultimate flexibility for the ultimate outcomes.

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SPECIAL FEATURE

The Complex Regulatory Landscape for Personalized Cancer Vaccines

Dr. Ilona Baraniak-Lang; Dr. Anna-Lena Amend

Advances in the cancer treatment space have renewed hope for breakthroughs with personalized cancer vaccines (often also called personalized immunotherapies). More recently, there have been promising results in a number of areas, including pancreatic cancer, melanoma, and non-small cell lung cancer (NSCLC).{1} According to analysts, significant growth is expected for cancer vaccines, with one report noting that the global market for cancer vaccines should grow from $10.21 billion in 2023 to $30.16 billion by the end of 2033.{2}

The principle behind personalized cancer vaccines is simple: the cancerous cells and healthy cells of the individual are genetically distinct.{3} The genetic alterations in tumor cells, specifically point mutations, often lead to the formation of cancer-specific neoantigens, which in turn can be utilized as highly specific targets for personalized immunotherapy. As personalized immunotherapy is tumor specific, it offers potentially novel, less toxic treatment options for patients{4} compared to many existing treatment options that affect both tumor and healthy cells, such as chemotherapy.

Another important feature of personalized cancer vaccines is the ability to elicit potent and durable anti-tumor immune response as well as creating immunological memory{1} and preventing cancer relapse.

Moreover, personalized cancer vaccines are not only used as a standalone treatment, but are also co-developed as reliable adjuvant therapies for immune checkpoint inhibitors (ICIs), as

the combination has a synergistic effect as well as the potential to overcome the ICI resistance in patients who are unresponsive.{5} A growing body of evidence demonstrates activity of the personalized cancer vaccines not only against highly immunogenic and immune-responsive tumors ("hot tumors") but also against non-immunogenic ("cold tumors"), which are normally resistant to immunotherapies.{6} Importantly, due to novel mode of action, personalized cancer vaccines represent hope for patients who have exhausted all other therapeutic options.

There are several options for developing a personalized immunotherapy product, including DNA, RNA, or peptides.{4} Additionally, cell-based products, such as autologous dendritic cell vaccines and viral vectors as a vaccine platform, are an emerging field.{7}

A plethora of clinical trials for (personalized) cancer vaccines are underway globally, with several in late-stage development.{8} However, as of now, very limited approved products are readily available for patients. In the European Union (EU), so far, no therapeutic cancer vaccine has been authorized. In the U.S., the Food and Drug Administration (FDA) has approved three therapeutic vaccines, with only one product, Provenge® (sipuleucel-T, approved in 2010) being a personalized product.{9} Provenge is a first-generation dendritic cell vaccine, which has, for example, been shown to improve median overall survival (OS) in advanced prostate cancer patients.

Regulatory Discrepancies

Despite the promise, our experience shows that there are many challenges that innovators need to overcome from a development, regulatory, and chemistry, manufacturing, and controls (CMC) perspective.

As a novel class of products, personalized cancer vaccines lack clear regulatory guidance, with regulatory standards and guidances still largely to be developed, which can result in a discrepancy in regulatory oversight and opinion of the regulatory agencies with regards to cancer vaccine development.{10} As such, certain approaches might be accepted by one agency but rejected by the other, which can result in divergent developments and even opposing regulatory opinions, making it very difficult for developers to follow a global approach.

Moreover, there are some major differences between the EU and U.S. in the classification of such products. While the FDA has introduced the term “therapeutic cancer vaccines” and classifies all of these products as such,{11} in the EU, there is no such specific classification available. The classification (and associated regulation) of these products depends on each product’s composition. For peptide or synthetic DNA/RNA products, products will likely be considered as vaccines and chemical medicinal products. However, nucleic acid-based products that are non-synthetic, dendritic cell vaccines or products using a viral vector are considered an advanced therapy medicinal product (ATMP) and ATMP regulations apply.{12} However, with an upcoming change in regulation, synthetic nucleic acids will likely also be considered ATMPs, which means the majority of cancer vaccines in the EU would be classified as ATMPs.{13}

The Role of Artificial Intelligence and Machine Learning

There are also major challenges with identifying the right target for the vaccine to ensure a good immunologic response. Here, artificial intelligence (AI), machine learning, and other bioinformatic tools are key.{14} To identify tumor-specific neoantigens, both healthy and tumor tissue samples are collected from cancer patients and subsequently analyzed in the lab by high throughput technologies, such as next-generation sequencing (NGS). Next, an (often proprietary) AI algorithm is used to identify unique antigens that are only expressed by the specific tumor and, at the same time exclude any targets present in healthy cells. This is critical, since inclusion of neoantigens that closely resemble targets in healthy cells could lead to autoimmunity and serious side effects for patients receiving a personalized cancer vaccine.{4}

With Moderna and Merck’s candidate mRNA-4157, for example, AI has been key in determining how the vaccine should be designed to target an individual patient’s cancer. Moderna expects the FDA will want to inspect its algorithm, given that AI is key to its development program.{15}

This does create some complexities, given the novel nature of AI-based development. However, further guidance on the use of AI and medicinal products is expected, with the FDA planning to release guidance on AI and machine learning in drug development this year.{16}

Given this complex and fast-changing environment, a multidisciplinary approach that brings together experts in vaccines, ATMPs, AI and machine learning, and knowledge of the regulatory requirements in both the U.S. and EU will be key.

Tackling CMC Challenges

One of the most complex issues for developers of personalized cancer vaccines to address is CMC (chemistry, manufacturing, and controls).

Firstly, it is important to note, that the currently established pharmaceutical paradigm was designed for drugs that are produced in bulk rather than for personalized medicines, where the product is different for each patient. As such, many currently existing regulations cannot be applied, or the traditional approaches must be modified and endorsed by the overseeing regulatory body.

Secondly, a fast turnaround is needed from biopsy to administration—typically under three months. This is key since these products are targeting late-stage cancer patients, so timing is critical. Nevertheless, such short timelines must cover several complex steps such as sample biopsy, drug-design, drug manufacture under Good Manufacturing Practice conditions, quality control, and drug distribution to a clinical site, all of which might be located in different geographies, and therefore requiring complex logistics. Streamlining the activities is extremely challenging since each product is unique and no common reference standard can be applied. Therefore, optimization of the processes, manufacture, and quality control of finished products needs to be performed, to a large extent, on the level of well-designed platform technology.

Use of Complex Bioinformatics Tools for Designing Investigational Medicinal Products

As previously noted, precision medicine follows a nonconventional production process, starting with the identification, selection, and preparation of patient-specific input material using NGS techniques and the vaccine design using AI and machine learning.{17} These are the areas that pose potential challenges for companies that are unfamiliar with detailed standards and requirements.

All NGS analysis must be conducted on validated protocols, with qualified equipment, and by trained staff. Processes should be accredited according to globally recognized standards,

including, for example, ISO 15189{18} for quality management specific to medical laboratories, ISO 17025{19} testing and calibration laboratory standards, College of American Pathologists (CAP) laboratory standards,{20} and onsite audits.

However, since NGS is well-established in clinical trials, these requirements are unlikely to be a major obstacle. The bigger challenge lies with AI and machine learning, since there is currently no internationally approved regulatory framework for assessing the use of these innovative algorithms in the design of these types of products. It is therefore difficult to predict exactly what will need to be provided. There is also a discrepancy between the major authorities. The FDA requires high-level information, including on all databases used to train the model and all detailed information regarding the bioinformatic tools used in this *in silico* pipeline,{21} while other regulators might not require similar level of detail on these novel bioinformatic tools.

Additionally, the informal advice given by the regulators is that the *in silico* pipeline should remain unchanged once the clinical trial application is submitted. The challenge here is that, because the system is self-learning, usually, acquired data are used to train and optimize it. Therefore, there needs to be a careful balance between the modifications and training of the system (which may also further improve it) and keeping it in a steady state, so that it is possible to make a comparison between clinical trials. To address this, developers will need to discuss with the regulators to what extent and when certain modifications can be introduced.

Potency

Another big challenge for CMC is how to establish the potency assay. These are normally used to quantitatively measure the biological activity of the drug in the disease-relevant system.{22} However, with personalized cancer vaccines there isn't a disease-relevant model as it will differ from patient to patient. Here, a potency assay would need to measure the neoantigen-specific T cell responses elicited by the vaccine, but to obtain a meaningful readout, these T cells would need to be collected from an already vaccinated patient. As such, a standard potency assay is not feasible and alternative solutions must be discussed with regulators beforehand.

Sterility Testing

One potential bottleneck is sterility testing. This is required for the release of finished products, but standard sterility testing takes at least two to three weeks to complete. This is critical, since the timeframe from biopsy to treatment should remain as short as possible to treat these late-stage cancer patients.

There are, however, several alternative options. One is to follow, where applicable, the principles of real-time release testing (more specifically parametric release), where testing is not performed on each batch (or each individual vaccine) but rather is dependent on demonstrating that pre-determined, validated sterilizing conditions have been achieved throughout the manufacturing process.{23} Here, experience shows that submission of evidence of successful validation of the manufacturing process and documentation on process monitoring during manufacturing, without direct measurement of quality attributes, is accepted.

Another approach might be to consider a "sterility by design" approach, leveraging a risk-based approach, where each step of the manufacturing process is designed to minimize any risk of microbial contamination.{24} Here, the enhanced product knowledge and process understanding, coupled with the use of quality risk management principles and the application of an appropriate pharmaceutical quality system, is critical to assure sterility of such products.

Another option would be to use alternative rapid sterility testing,{25} though this typically requires bringing in another service provider, which may not help to shorten the timeline.

In some situations, regulators may be open to allowing distribution to clinical sites without the final sterility test, on condition the results are provided as soon as possible and ensuring the product is not used at the clinical site before final release. In such cases, well-defined measures would need to be employed, such as detailed standard operating procedures, to ensure compliance with this approach.

Stability Barriers

The next big CMC challenge is stability testing. Since vaccines are personalized and can only be produced after enrolment of a patient in the trial, "traditional" stability testing is not

feasible. Developers must present well thought-out solutions to the regulators. Some approaches that we have seen regulators being open to include:

- Performing a range of studies where the manufacturer tests a whole spectrum of possible product make-up. For example, peptides where the developer may test the most hydrophobic and the most hydrophilic ones. Any other peptide that is produced using this system would fall within the range, which, experience shows, would provide confidence that the products will be stable.
- Investing in stability of several batches manufactured by the same process, for example, two engineering and five clinical batches.
- Leveraging prior knowledge of the platform technology. Specifically, with mRNA, the manufacturer may have stability data on similar products that use similar manufacturing processes and similar formulations. Our experience has found that this knowledge can be leveraged to provide greater assurance that the product will be stable.

Changing Regulatory Environment

The regulatory environment for personalized cancer vaccines continues to evolve alongside the science. So far, only a few guidances have been developed, and even when the regulators do release guidelines, the highly dynamic nature of the field means they are likely to be constantly updated.

Another big challenge is the lack of global harmonization, especially between major geographic regions, which means approaches accepted by some agencies may not be accepted by others. This can make it a difficult research space in which to navigate and define a harmonized global strategy.

It is therefore important that developers regularly engage with the authorities and seek their endorsement for any proposed solutions. Developers should also closely monitor guidances, position papers, and news in the field. Additionally, to address discrepancies between authorities, it is important to seek parallel or joint scientific advice—especially within the EU, where it is possible to leverage and use the opinion of one regulatory agency to inform another agency about the current plans.

Disclaimer

The information provided in this article does not constitute legal advice. PharmaLex and Cencora, Inc., strongly encourage readers to review available information related to the topics discussed herein and to rely on their own experience and expertise in making decisions related thereto.

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GOOD MANAGEMENT PRACTICE

Taking a Disruptive Approach to Getting New Treatments to Patients Faster: A Q&A with Andrew MacGarvey

Edited by Gary W. Cramer, Managing Editor for ACRP

Andrew MacGarvey, CEO and Founder of Coronado Research, which recently launched in the United Kingdom as a consultancy-led, professional services organization operating in the clinical development arena, has been involved in the clinical research enterprise for more 25 years. In his early career, he worked for a variety of contract research organizations in statistical programming and clinical data management. His interest in technology later took him to a software company when the evolution of electronic data capture was still very new, but for the last 16 years he has focused on data analytics and growing businesses with activities in the EMEA region, the United States, and Asia.

ACRP: What is the current climate like for startup companies servicing the clinical research enterprise?

MacGarvey: The current climate for the right startups is positive. Sponsor organizations are adopting new technologies and taking them in-house to gain control of, and derive extra value from, their data. As they navigate this transition, there is a place for speciality companies—first, to provide support around change management, and then ongoing execution capability as their customers embed the new solutions and processes into their development model. One key attribute these companies need is agility; the landscape is changing quickly, and startups are able to engage with the challenges without needing to evolve existing capabilities to meet the current models.

ACRP: What was your inspiration for the direction of Coronado Research, and what previous experiences gave you the foundation for its creation?

MacGarvey: I have spent my whole career in data services; it has become more and more apparent to me that sponsors could optimize the clinical development process by better leveraging the vast amount of data and metadata associated with clinical trials and beyond. I had seen use cases going live and making massive differences to my customers, and I started to think that if we could join the dots across the various stakeholders in development, there would be a real benefit for patients.

The data are critical assets; we now have the technology to access those data and the tools to bring the insights they hold to those charged with developing treatments and, crucially, those responsible for getting those treatments into markets worldwide. The true inspiration came from a chance meeting with a father who has set up a charitable foundation to search for a cure for his daughter, who has a rare disease. He has raised millions of dollars to help advance the science and now faces raising tens of millions more to run the clinical trials. When he told me his story and his race against time, I told him I would do whatever I could to help him. Those patients out there who, like his daughter, are waiting for treatments and cures need all of us to work tirelessly to accelerate the drug development process.

ACRP: In a press release about Coronado's activities, you had stated that the "blockbuster model isn't working." Why do you believe this is the case?

MacGarvey: This is linked very much to my previous answer. The current drug development process is well-worn, and we should recognize that it has delivered some amazing breakthroughs and dramatically increased safety for trial subjects. The problem is we developed the process in a world of blockbuster drugs, meaning widely recognized treatments with huge global markets.

However, science has moved very quickly; we are now in the world of increasingly personalized medicine and, in the case of rare diseases, very small patient populations. The "market" for new treatments is smaller (and in some cases very much smaller) than it was for much more common conditions. With the costs of drug development still increasing year-on-year and programs taking longer to complete, the shrinking market results in prohibitively expensive treatments—treatments which are approved but not taken up by payers, and worse,

potential treatments sitting on the laboratory bench because the economics don't work when coupled with the risk of failure.

These are all known problems; we now need to innovate to overcome them.

ACRP: Market changes can influence the success or failure of a new drug. How can we better forecast to ensure that not too much time or resources are invested into an investigational product that might fail? Let alone one that fails in the trial stage?

MacGarvey: We need to connect the dots from the regulatory stage for an investigational product through to commercialization of the approved product. As I have discussed, the challenge with people in our sector is that they all agree that we are still working in siloes in a big way. My hope is that data will be the "golden thread" that helps break through the barriers and bring teams together.

Now, we tend to focus solely on approval—especially in terms of what we need to do to get the submission accepted. When we have a successful submission, we then say, "OK, how are we going to get this into the market?" There are many examples of treatments coming in front of committees and being refused on cost grounds alone. We need to step back and work out how to get these treatments to the patients.

ACRP: What would you say are the biggest challenges facing the biopharmaceutical industry? And how can we better maximize the use of data and technology in clinical trials?

MacGarvey; There is a major challenge facing our industry, and it is here now. While we have a workable system for moving drugs from the laboratory to the patient, many of my peers agree it is becoming less fit for purpose. That is partially because of the move to more personalized or stratified medicine. But there is also the issue of ever-increasing volumes of data. We have not reached the inflexion point where we routinely use those data to accelerate the trial process; in fact, one might argue they are slowing the process down as we, as a profession, get to grips with artificial intelligence/machine learning. We must use the latest techniques to mine the data, and my ambition is to help drive change around the use of data to accelerate the development process and ultimately get treatments to patients faster.

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TRIALS & TECHNOLOGY

Enhancing Clinical Trials with Wearable Digital Health Technologies: Bridging the Gap Between Data and Real-Life Patient Experiences

Robin Harris

The integration of digital tools has brought better efficiency to clinical trials. Among these innovations, wearable devices are changing how data are collected, monitored, and analyzed. A growing shift toward digital endpoints paired with the widespread use of wearables has opened new avenues for real-world and more patient-centric data collection. The use of wearables also changes how study teams interact with their participants. Here, we look at the increasing role of wearables in clinical development, exploring their impact, benefits, and what they mean for researchers.

Growing Adoption of Wearables in Clinical trials

The increased use of wearable devices in clinical trials has coincided with improvements in their capabilities in recent years and the growing demand for more patient-centered assessments in development programs. Wearables like smartwatches and fitness trackers have allowed programs to monitor physiological parameters continuously. They place little to no burden on trial participants and provide researchers with access to more complete health data, tracking heart rate, blood pressure, glucose levels, and physical activity. They can also offer digital measures of sleep, mobility, and additional vital signs, including oxygen saturation and skin temperature.

Wearables collect data away from clinical settings, offering a more accurate assessment of patients' daily lives and reducing the need for frequent in-person site visits. They collect high volumes of data that provide a clearer picture of a specific medical condition than previously achievable using more traditional methods. Multiple studies using wearables have also shown high patient adherence of between 70% and 80%.

Better Insight into Diseases

Wearables are used in many medical conditions, especially in managing chronic diseases where continuous monitoring can provide a clearer picture of the lived experience of affected patients. In respiratory diseases, tracking physical activity and coughing symptoms can help researchers monitor idiopathic pulmonary fibrosis and chronic obstructive pulmonary disease.

Devices are being used to evaluate neurological conditions such as Parkinson's disease, where tracking symptoms such as tremors, gait disturbances, and sleep disruptions can be unreliable using in-clinic and at-home diary methods. Wearables can monitor movements and sleep disturbances, giving researchers better data on symptom fluctuations.

Using wearables to monitor activity levels and sleep patterns is also helpful in understanding the impact of novel weight loss medications. By capturing data on participants' physical activity and sedentary behavior, wearables can contribute to a more accurate assessment of change while receiving these treatments, helping researchers to better demonstrate and provide evidence of treatment efficacy.

Enhancing Engagement and Data Quality

Wearables can help keep participants engaged in a study for the duration of a clinical trial. They reduce the requirement for frequent in-clinic visits and make it easier for individuals to stay involved for long periods, if needed. Once a participant wears a device, the data immediately stream in, allowing researchers to monitor compliance in near real-time. This continuous engagement offers a much-needed opportunity for longitudinal programs that require consistent and robust data collection to assess the long-term outcomes of treatments. The wear periods for wearables can also be tailored to capture data at specific times. This could be around dosing or when a change in activity is expected.

Wearables enable trials to benefit from a round-the-clock assessment of participants rather than relying on periodic snapshots. This can ensure fluctuations and trends are identified that could easily go unnoticed using different tools.

Impact on Clinical Research Sites

Adopting wearables in clinical trials not only provides many advantages regarding data quality and efficiency, it can also bring certain additional considerations for research sites. While introducing unfamiliar steps may initially seem burdensome, multiple device assignment workflows can be tailored to meet a study team's specific needs and streamline the inclusion of wearables. This helps to minimize the demands on researchers' time. Electronic step-by-step guides are also provided for all workflows.

Researchers will need to become familiar with the software and be able to assign wearables accurately. They will also be required to fully understand the benefits of the devices and be comfortable with the study design, as they will be responsible for communicating this information to participants. Additionally, they will monitor wear compliance and ensure participants have all the necessary tools to maintain adherence.

Researchers will also be required to consider the visit structure and wear periods. Higher compliance is typically achieved when participants leave a site already wearing the device for the prescribed period.

Transitioning from traditional methods, such as patient questionnaires, to wearable-collected data can reduce the workload for researchers at clinical sites. While this shift decreases the time spent on manual data entry, wearables also present unique challenges.

One challenge is effectively communicating the value of participation to study participants, who are often blinded from their activity data to avoid influencing their behavior. This can make it challenging to demonstrate the value when participants are unaware of the science behind the data and the changes being captured. Study teams must clearly articulate how wearables contribute to the advancement of the trial and the improved understanding of the participant's disease.

The Future of Wearables in Clinical Research

Wearable technology in clinical trials is helping to improve how data are collected and used to support a study's aims. Real-time and continuous monitoring offers development programs and study teams valuable insights into participant health, helping to enhance the accuracy of clinical trial outcomes and broaden understanding of many different disease areas. Integrating

wearables in a study design can allow more people from broader geographies and varying backgrounds to access a clinical trial.

As clinical research moves toward more siteless or hybrid models with fewer in-person visits, there is a need to adapt to this by incorporating greater functionality through mobile apps and cellular data hubs. We are now seeing more data to support new wearable device capabilities, including battery life and data storage, verifying their use for extended wear periods.

The ongoing validation of wearables in clinical trials will continue to change how we design and conduct drug development programs, making studies more patient-centric and contributing to better insights. They hold the potential to improve not only how we collect data from participants, but also the type of data we collect and how we can use those data to inform the development of better treatments.

Robin Harris is Vice President of Client Services at ActiGraph. Since joining the company in 2015, she has played an integral role in the development of key internal processes to help operationalize digital health technologies in clinical trials. With extensive trial project management experience, she has a deep understanding of the complex operational challenges these technologies can introduce to a clinical development program, as well as proven strategies to successfully navigate this evolving landscape.

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