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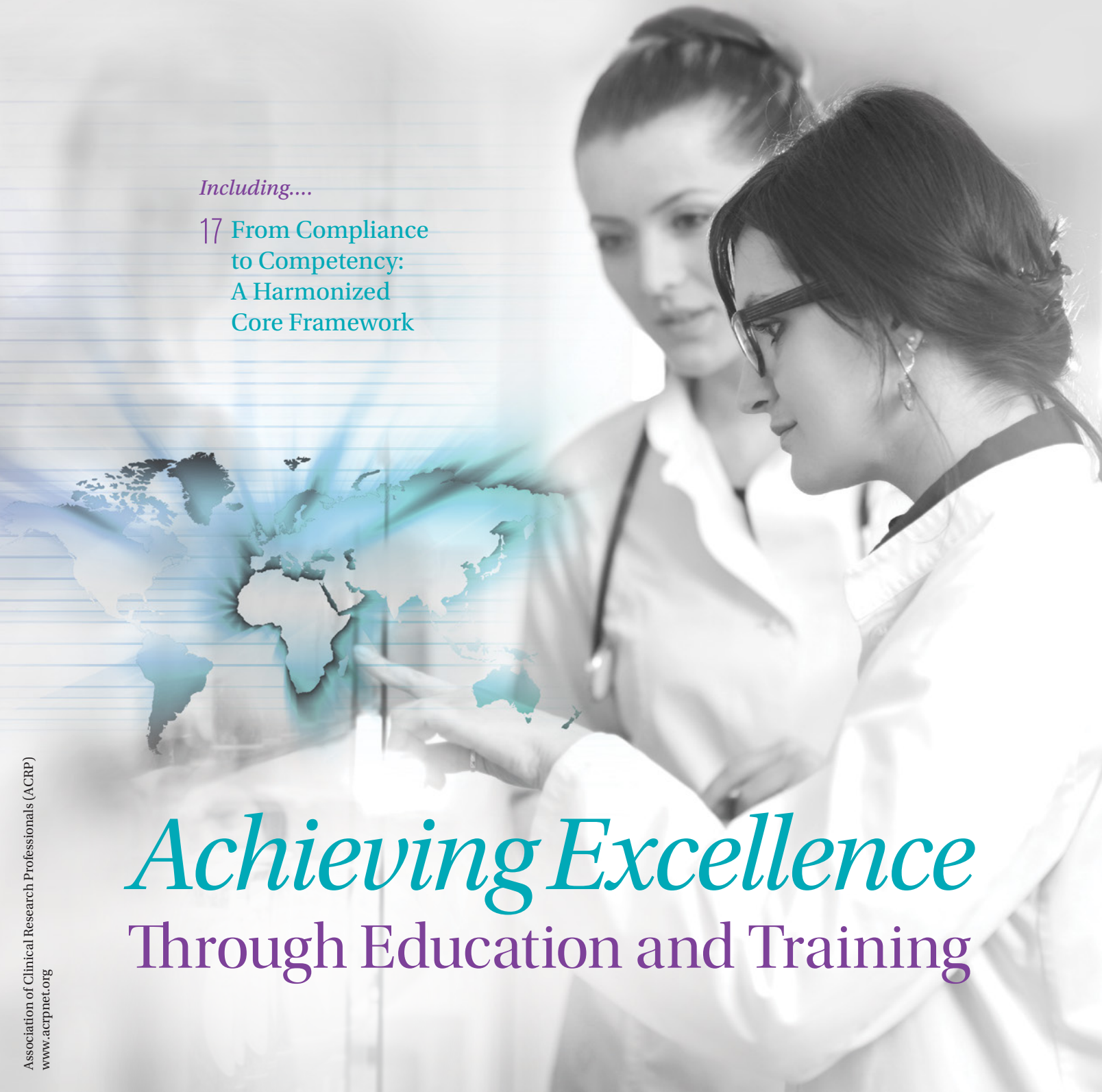

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GUEST EDITOR'S MESSAGE
Laurin Mancour, CCRA, CCRP

ACHIEVING EXCELLENCE
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Regulations, guidance, and ethical codes of conduct specify that clinical research professionals must be adequately trained and experienced before engaging in research with human subject participants.

The research community will continue to rely upon informed, trained, and educated stakeholders to move projects forward as new technologies, standards, and regulations evolve.

For example, in 1947, the ethical principles of the Nuremberg Code[1] first described that research with human subjects should be conducted only by scientifically qualified persons who will conduct experiments with the highest degree of skill and care. Later, the basic principles of the World Medical Association's Declaration of Helsinki[2] stated that medical research should be conducted only by competent, appropriately qualified professionals with applicable ethics, scientific education, and training. Current U.S. regulations (21 CFR 312 Subpart D in the *Code of Federal Regulations*)[3] also require principal investigators and professionals monitoring clinical trials to be qualified through sufficient training and experience.

What is Needed, and Why

Competent, well-trained personnel are needed to manage complex clinical trials. Talented professionals may achieve suitable levels of education and experience to enter the research field, but they must be trained to industry standards if they wish to perform job functions in a way that promotes quality, mitigates risk, and advances medical science.

Individuals engage in a variety of professional development efforts to improve their knowledge, skills, and abilities so that they will be effective in a business role. To demonstrate regulatory compliance and improve the conduct and performance of research activities, organizations monitor staff training needs and ensure that knowledge gaps are addressed.

Institutional training can also be a practical strategy for improving providers' engagement in and understanding of research initiatives. An organizational culture that promotes research awareness through training gives practitioners tools to effectively communicate information about research opportunities and results to patients to safeguard their interests.

Talented professionals may achieve suitable levels of education and experience to enter the research field, but they must be trained to industry standards if they wish to perform job functions in a way that promotes quality, mitigates risk, and advances medical science.

Updates made in 2013 to the Declaration of Helsinki clearly state that "…all medical research subjects should be given the option of being informed about the general outcome and results of the study."[2] The 2014 revision to the European Union Clinical Trials Directive[4] requires sponsors to report study results within one year of the end of the clinical trial. Detailed summaries of clinical trials data, including summaries in lay language, are being centralized on publicly accessible websites for the purposes of educating the public and informing them about specific trials.

Educating study subjects about their participation empowers them with information about their health. Disclosing study information informs subjects about their contribution to medical science and encourages participation in future clinical trials. As industry is struggling to comply with new, global regulatory requirements for disclosing trial results, amendments to the Food, Drug, and Cosmetic Act[5,6] have prompted institutions to foster training on adjusting end-of-study practices so that site staff may improve communication with participants about study outcomes.

Where We're Going, and How to Get There

Education and training of professionals have been a focus of the research community since 1947. The scope of research regulations has expanded to include responsibilities for educating society. The public has come to be recognized and respected as a vital stakeholder, empowered to make informed decisions about research.

As clinical research becomes less centralized, global agencies need ever-increasing standardization and harmonization of information in order to function effectively. There is a critical need to build an infrastructure that supports training on research ethics, new standards, and emerging regulations. Collaborative professional networks provide systems and resources for understanding the practical skills that are needed to improve trial safety, quality, and efficiency. Professional organizations have also become useful clearinghouses for training resources and information exchange in this environment.

The research community will continue to rely upon informed, trained, and educated stakeholders to move projects forward as new technologies, standards, and regulations evolve. However, our industry is beginning to experience a talent pipeline crisis in certain functional areas (e.g., pharmacovigilance, monitoring, etc.), since there are not enough professionals to meet desired skills and qualifications for these positions. Building a skilled workforce is integral to advancing the clinical research profession and safeguarding the volunteers who participate in trials.

The Association of Clinical Research Professionals (ACRP)[7] has created development pathways for professionals to understand the knowledge and skills required for specific professional roles. This roadmap identifies where proficiency and mastery of discrete competency areas are anticipated as responsibilities increase, so that professionals can identify ongoing areas for growth.

ACRP has designed a comprehensive professional development program with innovative eLearning opportunities to meet educational needs and promote the success of students. Its nationally accredited certification program also provides global recognition for eligible professionals who demonstrate their expertise by passing standardized examinations.

Conclusion

Remaining mindful of educational expectations for professional qualification and accountability is the best tool to ensure that our industry is prepared for the practical reality of an ever-changing, global research environment. To live up to the ideals and aspirations that we have for our industry, organizations, subject participants, and society, we have institutionalized training efforts and developed standards for assessing professional competence.

Embracing a learning culture that anticipates institutional change allows us to constantly improve our professional foundations to improve service to our industry, institutions, participant volunteers, and the public. This, in turn, serves to elevate us all.

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Jamie Meseke, MSM, CCRA | Rielle Illy, BS

Balancing Professional and Personal Responsibilities
(or How to Stay Afloat as a Traveling CRA)

CNNMoney named the clinical research associate (CRA) position as one of the "10 Best Jobs in America" for 2012 and 2013, and the demand for CRAs is expected to grow over the next decade.[1] Although the position can be very rewarding and exciting, the expectations placed on CRAs by various stakeholders (e.g., sponsors/contract research organization [CRO] management/investigative sites) may contribute to the perceived high level of attrition across the industry.

Professional burnout is a frequently cited reason for CRA turnover. Major predictors of burnout may include the high number of working hours, work/home conflicts, and acceptance of additional tasks outside the normal job duties.[2] A cursory search of the Internet yields a plethora of commentary and inquiry from CRAs across the world interested in learning tips of the trade from their peers with regard to maximizing professional efficiency and career advancement while avoiding burnout.

Identifying Professional and Personal Stakeholders

It can be difficult to recognize when burnout is looming and when the work/life relationship is imbalanced. CRAs should periodically gauge whether (re)alignment may be necessary by taking time to identify the stakeholders and obligations they have in both their professional and personal pursuits, in order to devise a workable (and sustainable) strategy for striking balance between competing demands on their time. Professional obligations can range from project-specific needs, such as preparing for data locks and keeping up with visit reports and follow-up letters, to more general job-related responsibilities like training, expense account reconciliation, continuing education, and career goal-planning.

Typical pitfalls that lead to burnout include the ever-growing list of responsibilities and lack of hours in the day to complete all tasks. Some CRAs accept unrealistic site loads and travel schedules in order to gain experience in the industry. Others may be uncomfortable or inexperienced with saying "no" when asked to take on additional tasks. However, as Oxman and Sackett point out, "The issue is that by saying 'yes' too often, you run the risk of overcommitment, overwork, underachievement across the board, undersocialization, underenjoyment, failure to deliver on your commitments, and burnout."[2]

An overwhelming list of job duties and expectations may cause a CRA to allot very little, if any, time for personal obligations and interests. Because work/life imbalance is a major contributor to burnout, it is important mentally and physically for CRAs to devote sufficient time to interests outside work.

Based on more than 10 years of experience as traveling CRAs with competing business and personal interests, we have devised a strategic approach for striking work/life balance. The process begins with identifying personal stakeholders and obligations (see Figure 1).

Jamie Meseke, MSM, CCRA | Rielle Illy, BS

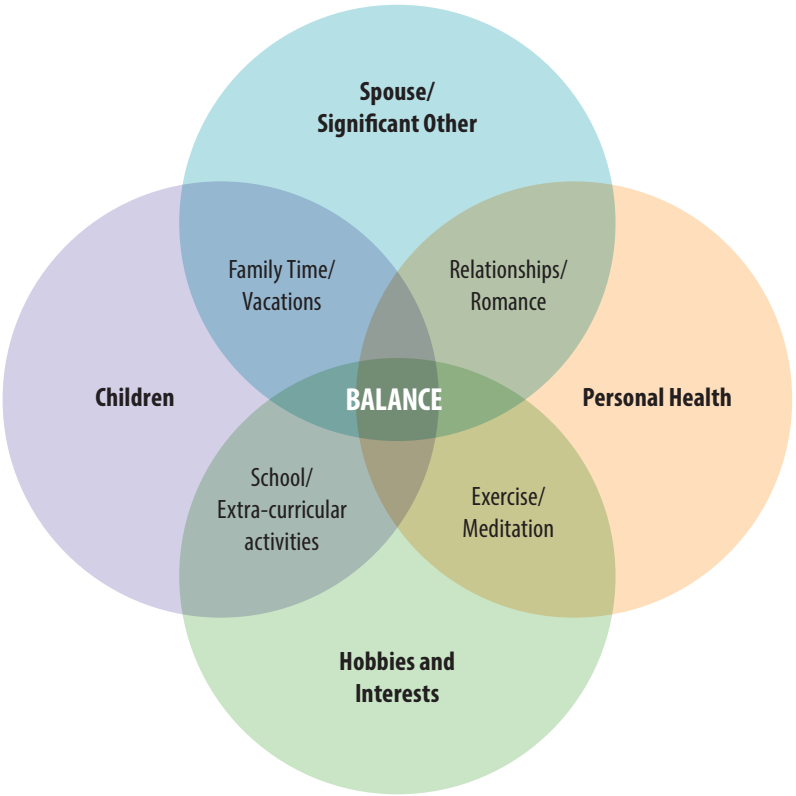
It can be difficult to recognize when burnout is looming and when the work/life relationship is imbalanced.

Setting Priorities

Once all stakeholders and significant obligations have been identified, CRAs should prioritize their obligations according to present needs and demands. They should re-evaluate the prioritized list at periodic intervals, and shift priorities up or down as needs warrant. Here is a sample CRA priorities list:

1. Devote more attention to spouse or significant other
2. Identify new ways to connect with children or friends while on the road
3. Research exercise or healthier eating options at home and while traveling
4. Schedule time for hobby or personal enrichment activities
5. Pursue advanced degree or career advancement

FIGURE 1. Examples of Personal Stakeholders and Obligations



Many CRAs find that once the personal stakeholders have been identified and prioritized, it is much easier to focus on individual areas:

- As important as it is to have open and continuous communication with management at work, it is also vitally important to maintain open communication with your spouse and loved ones with regard to travel and work commitments.
- Establish a strong support system to help when challenges arise.
- Solicit extended family members to help transport kids to extracurricular activities when you are out of town.
- If you know someone with a flexible schedule, ask him or her to walk your dog or check on your cats during the day.
- Getting help from extended family and friends can lessen the burden on spouses and significant others.

Making it Work

We have compiled a list of effective tips to help balance professional and personal interests. Although this list is far from comprehensive, individual CRAs can adapt the general idea to suit themselves. These tips should be used as launching points for creating personal plans.

Conclusion

The life of a traveling CRA can be hectic and downright lonely at times. By using time efficiently and effectively while on the road, CRAs can devote more time to family, friends, and personal interests while at home.

Balancing the demands of work and home life may continue to be challenging. However, identifying and prioritizing personal stakeholders and obligations is a critical step toward generating a workable strategic plan. Incorporating even just a few of these tips may enable you to take control and action over the work/life struggle.

Some CRAs accept unrealistic site loads and travel schedules in order to gain experience in the industry.

Tips for Work/Life Balance

- Use travel time for work-related duties, when possible. Time on the plane or at the airport may be used to draft reports and follow-up letters or complete job-related training.
- Loop visits together, when possible, to save time and money.
- During onsite visits, complete reports and follow-up letters as much as possible in real-time. This makes for less post-visit work and helps ensure details are documented while they are fresh in your mind.
- Create a weekly or monthly schedule to keep track of important appointments, school activities, birthdays, etc. Keep copies at home and with you when you travel.
- Develop a menu plan. Many CRAs find that menu planning allows them to ensure their families eat healthy while they are traveling. Personal menu planning may also help CRAs develop their own healthy eating habits. A little research prior to traveling each week can help CRAs avoid constantly grabbing a meal from the nearest fast food venue. Menu planning can also significantly reduce food-related expenses.
- Use frequent-flier and hotel rewards to book family vacations or long weekends with your spouse or significant other.
- Exercise on the road! Most hotels offer work-out facilities, but exercise does not have to take place in a formal setting. Something as simple as taking a brisk walk around the hotel or the investigative site can boost mental energy and raise the heart rate. Exercise can also be done in the comfort of your hotel room. Check out youtube.com for a never-ending supply of yoga, Pilates, and aerobic exercise videos.
- If you are enrolled in a degree program or pursuing continuing education, try to study on the road or while traveling to allow for more time at home for family, friends, and personal interests.
- Take time for hobbies and pleasure, as well as general health and well-being. Many hobbies, like photography, knitting, or reading, can easily be taken with you when you travel.
- Give family and friends something to look forward to when you return. Simple souvenirs can go a long way to easing misgivings about the time you spend away from home.
- Spend time doing something fun and focused on the family when you return home.

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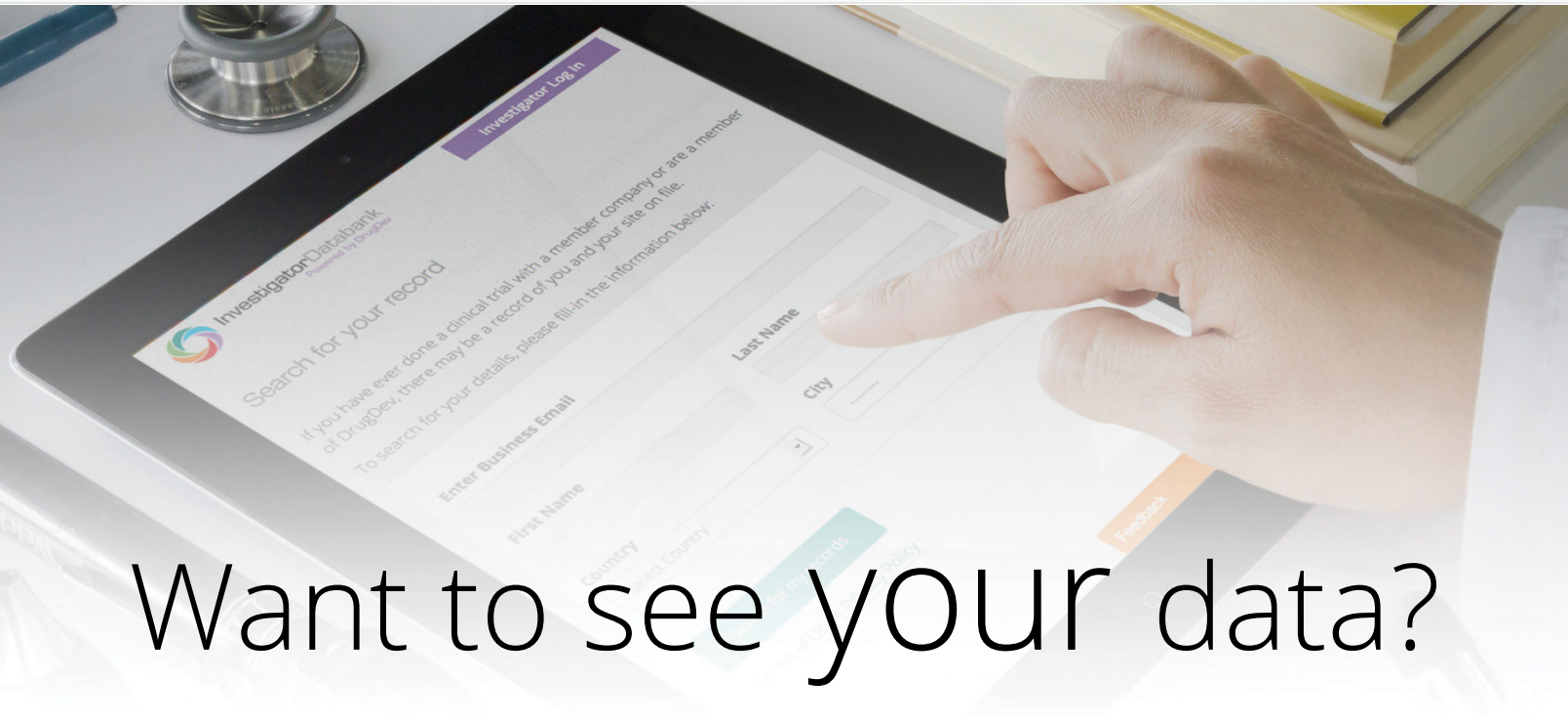

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Moving from Compliance to Competency: *A Harmonized Core Competency Framework for the Clinical Research Professional*

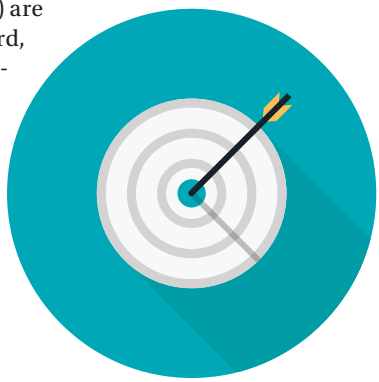
PEER REVIEWED | Stephen A. Sonstein, PhD | Jonathan Seltzer, MD, MBA, MA, FACC | Rebecca Li, PhD | Honorio Silva, MD | Carolynn Thomas Jones, DNP, MSPH, RN | Esther Daemen, BSN, PG, PMP, MBA

[DOI: 10.14524/CR-14-00002R1.1]

Medicines development and clinical research are among the most heavily regulated activities on a global basis. As our understanding of pathophysiology and therapeutic intervention has increased, there has been a concomitant increase in the complexity of clinical trial protocol requirements[1] and in the number and complexity of the regulations and guidelines related to the preclinical and clinical testing of new drugs and devices.[2]

Quite curiously, though, only very general requirements and scant detail in the regulatory authority definitions exist for the criteria required of the individuals who are responsible for the conduct of clinical trials with human subjects. Previous versions of the Declaration of Helsinki[3] and the International Conference on Harmonization's Guideline for Good Clinical Practice (ICH GCP) E6[4] list only vague requirements for education and experience.

In most countries, anyone with a medical license can serve as a principal investigator of a clinical trial, regardless of whether he/she has had previous training or experience in clinical research. Certification programs for principal investigators (PIs), clinical research coordinators (CRCs), and clinical research associates (CRAs) are held in high regard, but no formal regulations define the educational or experiential requirements for, or mandate certification in, the conduct of clinical trials.



Turning of the Tide

The tide is beginning to turn, however. The latest version of the Declaration of Helsinki, dated October 2013, now states that "medical research must be conducted by individuals with appropriate training and qualifications in clinical research."[3] India has mandated certification for clinical investigators, but it is uncertain what competencies such certification will require. Also, many professional organizations have developed training programs for individuals who conduct clinical trials, and some clinical institutions require clinical research training as a prerequisite for participation on research teams.[5]

During the last decade, academic institutions have developed programs that award advanced degrees in clinical research, clinical trial management, and regulatory affairs.[6] Although one can infer that education and training will enhance the level of regulatory compliance, we have been unable to translate this into a measurement of competence. This is perhaps because there is no systematic harmonization of job descriptions and performance outcomes for the many roles that exist in the clinical research enterprise. Recently, several professional groups related to the clinical research enterprise published articles and white papers or presented content at professional meetings to bring this message to light.[7–10]

LEARNING OBJECTIVE
After reading this article, participants should be able to explain the value of developing a harmonized framework of core competencies required for the conduct of high-quality, safe, and ethical clinical research.

DISCLOSURES
Stephen A. Sonstein, PhD; Jonathan Seltzer, MD, MBA, MA, FACC; Rebecca Li, PhD; Honorio Silva, MD; Carolynn Thomas Jones, DNP, MSPH, RN: Nothing to Disclose
Esther Daemen, BSN, PG, PMP, MBA: Employee of ACRP

Joint Task Force for Clinical Trial Competency Contributors and Collaborators

Academy of Physicians in Clinical Research

Association of Clinical Research Professionals

Amgen

Alliance for Clinical Research Excellence and Safety

Clinical & Translational Science Awards

Clinical Trials Transformation Initiative

Collaborative Institutional Training Initiative

Consortium of Academic Programs in Clinical Research

Deloitte

Drug Information Association

Global Health Network

Inter-American Foundation for Clinical Research

International Academy of Clinical Research

International Federation of Associations of Pharmaceutical Physicians

Korea National Enterprise for Clinical Trials

MAGI

Multi-Regional Clinical Trial Center

Pfizer

PharmaTrain

TransCelerate Biopharma, Inc.

UK Clinical Research Collaboration

As the concept of competency-based education and training has spread to the medicines development industry, many groups have produced a list of knowledge, skills, and attitudes defining the core competencies required of the clinical research professional. For the most part, the approach of each group has been focused on a specific component of the clinical research enterprise. Some examples are:

- The National Center for Advancing Translational Sciences (part of the National Institutes of Health) in the U.S., which has developed listings of core competencies for translational research scientists;[11]
- The International Federation of Associations of Pharmaceutical Physicians and the Academy of Physicians in Clinical Research (APCR), which have developed listings of core competencies for pharmaceutical physicians and clinical investigators;[12,13]
- The Consortium of Academic Programs in Clinical Research, which has developed core competencies for graduates of academic programs and to guide curriculum development;[7]
- The Association of Clinical Research Professionals (ACRP), which has defined a career development pathway for CRCs, CRAs, and PIs incorporating competency statements;[14] and
- The Regulatory Affairs Professionals Society, which has adopted core competency statements that relate to regulatory affairs professionals.[15]

Furthermore, professional nursing in the U.S. and United Kingdom has contributed to this effort through a variety of clinical research role delineation studies and competency-defining publications.[16–20] These combined efforts have begun the process of moving the clinical research enterprise from a focus on regulatory compliance to a focus on professional competency.

Coalescing on Competency

In an attempt to bring together these disparate, but high-quality efforts focused on clinical trial competence, a meeting of representatives from pharmaceutical companies, contract research organizations, academic institutions, clinical research sites, and professional societies was hosted by the Multi-Regional Clinical Trial (MRCT) Center at Harvard University during spring 2013. A broad-based and widely representative group was formed and named the Joint Task Force (JTF) for Clinical Trial Competency.

The members of the JTF agreed to work toward aligning and harmonizing the many focused statements relating to core competency for clinical research professionals into a single, high-level set of standards, which could be adopted globally and serve as a framework for defining professional competency throughout the clinical research enterprise. The JTF had a second face-to-face meeting in June 2013, which included participants from an even broader representation of the clinical research community.

A listing of the JTF's collaborating organizations is found in the sidebar. The JTF then worked through the summer of 2013 and presented its final report in October of that year.

The process used by the JTF was designed to acknowledge and incorporate the inputs from the many participating organizations. It required a review of the many different competency statements and identification of competency domains, or broad categories of the knowledge, skills, and attitudes necessary to function within the field of clinical research. It determined that all of the competency statements could be aligned within the eight competency domains listed in Figure 1.

The members of the JTF agreed to work toward aligning and harmonizing the many focused statements relating to core competency for clinical research professionals into a single, high-level set of standards, which could be adopted globally and serve as a framework for defining professional competency throughout the clinical research enterprise.

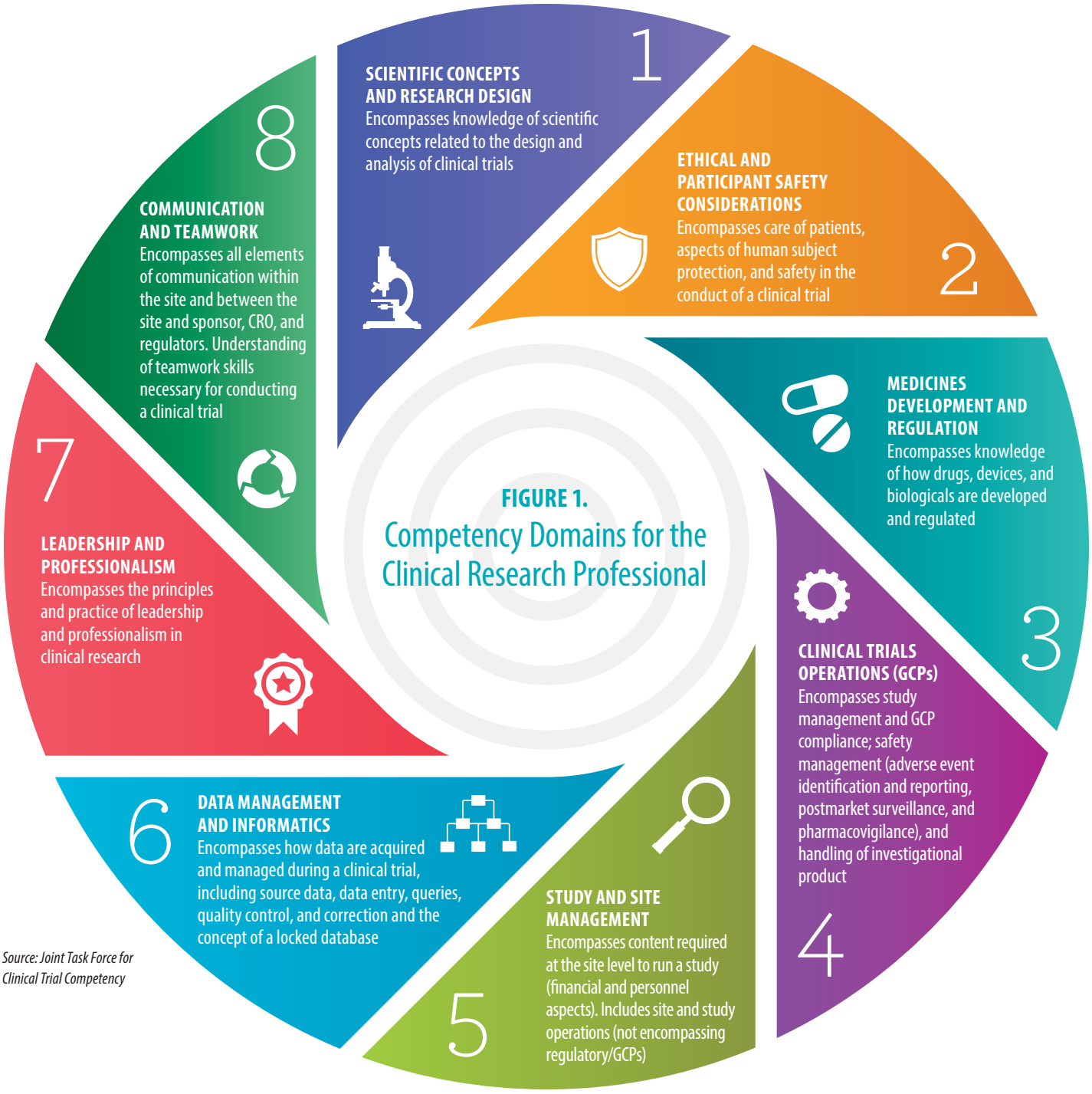


FIGURE 1.
Competency Domains for the Clinical Research Professional

Source: Joint Task Force for Clinical Trial Competency

The next step required focusing on the individual statements of knowledge, skill, and attitude (KSA) learning objectives from each of the many publications and presentations and aligning them within the appropriate competency domain. The final step involved reviewing all of the KSA learning objective statements within each competency domain and harmonizing them, so that the wording of the final KSA statements was inclusive and represented each individual organization's priorities, but was not redundant or repetitive.

The JTF decided that the harmonized competency statements at this level should reflect primarily cognitive skills, and that the performance or attitudinal aspects of learning objectives were best defined at a more granular level by groups that would use the statements as a Core Competency Framework to further develop focused expressions for specific components of the enterprise (e.g., job descriptions, accreditation criteria, training requirements). The JTF and collaborating organizations then systematically reviewed the proposed competencies and domains, integrating comments and suggestions into the final product, which is presented in Table 1.

The Core Competency Framework can be used in many ways toward improving the quality and safety of the clinical research enterprise.

TABLE 1. Harmonized Core Competencies for the Clinical Research Professional

SCIENTIFIC CONCEPTS AND RESEARCH DESIGN

- Demonstrate knowledge of pathophysiology, pharmacology, and toxicology as related to medicines discovery and development
- Identify clinically important questions that are potentially testable clinical research hypotheses, through review of the professional literature
- Explain the elements (statistical, epidemiological, and operational) of clinical and translational study design
- Design a clinical trial
- Critically analyze study results with an understanding of therapeutic and comparative effectiveness

ETHICAL AND PARTICIPANT SAFETY CONSIDERATIONS

- Compare and contrast clinical care and clinical management of research participants
- Define the concepts of "clinical equipoise" and "therapeutic misconception" as related to the conduct of a clinical trial
- Compare the requirements for human subject protections and privacy under different national and international regulations and ensure their implementation throughout all phases of a clinical study
- Explain the evolution of the requirement for informed consent from research participants and the principles and content of the key documents ensuring the protection of human participants in clinical research
- Describe the ethical issues involved when dealing with vulnerable populations and the need for additional safeguards
- Evaluate and apply an understanding of the past and current ethical issues, cultural variations, and commercial aspects to the medicines development process
- Explain how inclusion and exclusion criteria are included in a clinical protocol to assure human subject protection
- Summarize the principles and methods of distributing and balancing risk and benefit through selection and management of clinical trial subjects

MEDICINES DEVELOPMENT AND REGULATION

- Discuss the historical events that precipitated the development of governmental regulatory processes for drugs, devices, and biologics
- Describe the roles and responsibilities of the various institutions participating in the medicines development process
- Explain the medicines development process and the activities that integrate commercial realities into the life cycle management of medical products
- Summarize the legislative and regulatory framework that supports the development and registration of medicines, devices, and biologics and ensures their safety, efficacy, and quality
- Describe the specific processes and phases that must be followed in order for the regulatory authority to approve the marketing authorization for a medical product
- Describe the safety reporting requirements of regulatory agencies both pre- and post-approval
- Appraise the issues generated and the effects of global expansion on the approval and regulation of medical products

CLINICAL TRIALS OPERATIONS (GCPs)

- Evaluate the conduct and management of clinical trials within the context of a Clinical Development Plan
- Describe the roles and responsibilities of the clinical investigation team as defined by GCP guidelines
- Evaluate the design conduct and documentation of clinical trials as required for compliance with GCP guidelines
- Compare and contrast the regulations and guidelines of global regulatory bodies relating to the conduct of clinical trials
- Describe appropriate control, storage, and dispensing of investigational products
- Differentiate the types of adverse events (AEs) that occur during clinical trials, understand the identification process for AEs, and describe the reporting requirements to institutional review boards/independent ethics committees (IRBs/IECs), sponsors, and regulatory authorities
- Describe how global regulations and guidelines assure human subject protection and privacy during the conduct of clinical trials
- Describe the reporting requirements of global regulatory bodies relating to clinical trial conduct
- Describe the role and process for monitoring of the study
- Describe the roles and purpose of clinical trial audits
- Describe the safety reporting requirements of regulatory agencies both pre- and post-approval
- Describe the various methods by which safety issues are identified and managed during the development and postmarketing phases of clinical research

STUDY AND SITE MANAGEMENT

- Describe the methods utilized to determine whether or not to sponsor, supervise, or participate in a clinical trial
- Develop and manage the financial, timeline, and cross-disciplinary personnel resources necessary to conduct a clinical or translational research study
- Apply management concepts and effective training methods to manage risk and improve quality in the conduct of a clinical research study
- Utilize elements of project management related to organization of the study site to manage patient recruitment, complete procedures, and track progress
- Identify the legal responsibilities, issues, liabilities, and accountabilities that are involved in the conduct of a clinical trial
- Identify and explain the specific procedural, documentation, and oversight requirements of PIs, sponsors, contract research organizations (CROs), and regulatory authorities related to the conduct of a clinical trial

DATA MANAGEMENT AND INFORMATICS

- Describe the role that biostatistics and informatics serve in biomedical and public health research
- Describe the typical flow of data throughout a clinical trial
- Summarize the process of electronic data capture and the importance of information technology in data collection, capture, and management
- Describe the ICH GCP requirements for data correction and queries
- Describe the significance of data quality assurance systems and how standard operating procedures are used to guide these processes

LEADERSHIP AND PROFESSIONALISM

- Describe the principles and practices of leadership, management, and mentorship, and apply them within the working environment
- Identify and implement procedures for the prevention or management of the ethical and professional conflicts that are associated with the conduct of clinical research
- Identify and apply the professional guidelines and codes of ethics that apply to the conduct of clinical research
- Describe the effect of cultural diversity and the need for cultural competency in the design and conduct of clinical research

COMMUNICATION AND TEAMWORK

- Discuss the relationship and appropriate communication between sponsor, CRO, and clinical research site
- Describe the component parts of a traditional scientific publication
- Effectively communicate the content and relevance of clinical research findings to colleagues, advocacy groups, and the nonscientist community
- Describe methods necessary to work effectively with multidisciplinary and inter-professional research teams

Implementing the Core Competency Framework

The Core Competency Framework can be used in many ways toward improving the quality and safety of the clinical research enterprise, such as to define certification criteria used by personnel or site certifying agencies. The framework also could be used to formulate accreditation standards for academic programs, both to standardize curricula and to ensure that programs are sufficiently comprehensive.

Ultimately though, the most effective method to improve clinical trials would be to ensure that those responsible for the various aspects of the clinical trial bring the appropriate competence at the appropriate time. The greater challenge is implementation of this conceptual framework into an operational model, and a good place to start could be the clinical research design, whereby a look at competencies across two different types of studies can reveal variability in requirements.

For instance, comparing an investigator-initiated, observational trial to an industry-sponsored, premarket interventional trial illustrates how this framework might be used to qualify a PI. As depicted in Table 2, the competencies for the Study and Site Management Domain are identical in the two different styles of trial, but not so for the Scientific and Research Design Domain. This does not imply that a less competent investigator can perform an observational study, but that a lower level of competency is required for that study method. Furthermore, the level of competency might be quite different for other clinical research team roles, such as CRC, CRA, data manager, or regulatory affairs coordinator.

Once the necessary competency is defined, the PI, study sponsor, and interested regulatory authority must ensure that the study team member possesses the necessary competencies to carry out the selected, protocol-defined tasks. If additional knowledge or skills are needed, this would be the proper place to integrate with training programs that have training materials and processes that are harmonized to the protocol-specific competency requirements.

As a second example, Table 3 illustrates how one could use the Core Competency Framework to define the ICH GCP knowledge requirements for an interventional clinical trial based on the functional roles of a PI, CRC, or CRA.

TABLE 2. Competencies and Study Methods

DOMAIN	STUDY METHOD	
Scientific and Research Design	**Observational**	**Interventional**
Demonstrate knowledge of pathophysiology, pharmacology, and toxicology as they relate to medicines discovery and development	Optional	Required
Identify clinically important questions that are potentially testable clinical research hypotheses, through review of the professional literature	Required	Optional
Explain the elements (statistical, epidemiological, and operational) of clinical and translational study design	Required	Required
Design a clinical trial	Required	Optional
Critically analyze study results with an understanding of therapeutic and comparative effectiveness	Optional	Optional
Study and Site Management		
Describe the methods used to determine whether or not to sponsor, supervise, or participate in a clinical trial	Required	Required
Develop and manage the financial, timeline, and cross-disciplinary personnel resources necessary to conduct a clinical or translational research study	Required	Required
Describe the reporting requirements of global regulatory bodies relating to clinical trial conduct		
Apply management concepts and effective training methods to manage risk and improve quality in the conduct of a clinical research study	Required	Required
Use elements of project management related to organization of the study site to manage patient recruitment, complete procedures, and track progress	Required	Required
Identify the legal responsibilities, issues, liabilities, and accountability that are involved in the conduct of a clinical trial	Required	Required
Identify and explain the specific procedural, documentation, and oversight requirements of PIs, sponsors, CROs, and regulatory authorities that relate to the conduct of a clinical trial	Optional	Required

Not all members of the clinical research team require the highest level competency in all of the areas listed, but these harmonized core competencies can provide a basis for development of specific statements of knowledge, skills, and attitudes required by clinical research professionals in focused environments.

TABLE 3. Competencies by PI, CRC, and CRA Roles

DOMAIN	PI Role	CRC Role	CRA Role
Clinical Trial Operations			
Evaluate the conduct and management of clinical trials within the context of a Clinical Development Plan	Required	Optional	Optional
Describe the roles and responsibilities of the clinical investigation team as defined by GCP guidelines	Required	Required	Required
Evaluate the design conduct and documentation of clinical trials as required for compliance with GCP guidelines	Required	Optional	Required
Compare and contrast the regulations and guidelines of global regulatory bodies relating to the conduct of clinical trials	Required	Optional	Required
Describe appropriate control, storage, and dispensing of investigational products	Required	Required	Required
Differentiate the types of AEs that occur during clinical trials, understand the identification process for AEs, and describe the reporting requirements to IRBs/IECs, sponsors, and regulatory authorities	Required	Required	Required
Describe how global regulations and guidelines assure human subject protection and privacy during the conduct of clinical trials	Required	Optional	Optional
Describe the reporting requirements of global regulatory bodies relating to clinical trial conduct	Required	Optional	Optional
Describe the reporting requirements of global regulatory bodies relating to clinical trial conduct	Required	Optional	Optional
Describe the role and process for monitoring of the study	Required	Optional	Required
Describe the roles and purpose of clinical trial audits	Required	Optional	Required
Describe the safety reporting requirements of regulatory agencies both pre- and post-approval	Required	Required	Required
Describe the various methods by which safety issues are identified and managed during the development and post-marketing phases of clinical research	Optional	Optional	Optional
Study and Site Management			
Describe the methods used to determine whether or not to sponsor, supervise, or participate in a clinical trial	Required	Optional	Optional
Develop and manage the financial, timeline, and cross-disciplinary personnel resources necessary to conduct a clinical or translational research study	Required	Optional	Optional
Apply management concepts and effective training methods to manage risk and improve quality in the conduct of a clinical research study	Required	Optional	Optional
Use elements of project management related to organization of the study site to manage patient recruitment, complete procedures, and track progress	Required	Required	Optional
Identify the legal responsibilities, issues, liabilities, and accountabilities that are involved in the conduct of a clinical trial	Required	Required	Required
Identify and explain the specific procedural, documentation, and oversight requirements of PIs, sponsors, CROs, and regulatory authorities related to the conduct of a clinical trial	Required	Optional	Required

Summary

The mission of this JTF initiative has been to bridge the gap between "what to do" and "how to do it." For the first time, a universally applicable, globally relevant framework exists that identifies the competency domains and the associated cognitive skills necessary to conduct a high-quality, ethical, and safe clinical trial.

Not all members of the clinical research team require the highest level competency in all of the areas listed, but these harmonized core competencies can provide a basis for development of specific statements of knowledge, skills, and attitudes required by clinical research professionals in focused environments. The leveling of competencies from novice to expert—or by professional role—can be a next step in this endeavor.

Competency-based curricula or job descriptions can lead to standardization and elimination of redundancy in training requirements, standardization and accreditation of educational programs, and definition of career tracks and performance evaluations. The sidebar lists several of the possible uses and outcomes that can result from the adoption and use of the Core Competency Framework by the clinical research enterprise and global regulatory authorities.

The JTF aims to approach the regulatory bodies of the world for recognition and acknowledgment of the Core Competency Framework, and ultimately to house the document and its future evolutions within the ICH as a guideline similar to ICH GCP E6.[4]

Acknowledgments

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Potential Uses and Outcomes of a Harmonized Core Competency Framework, for Standardizing and Streamlining

- Curriculum development
- Training initiatives
- Basic training requirements
- Investigator approvals
- Guidance for IRB approvals
- Site approvals and selection
- Study coordinator delegation
- Study monitor roles
- Defining clinical research career ladders and levels
- Job descriptions and performance evaluations
- Policy development
- Regulatory compliance
- Quality improvement
- Academic program and site accreditation
- Academic requirements for clinical research roles
- Professional certification
- Bridging gaps in innovation exchange
- Infusing improved performance outcomes into the global clinical research enterprise workforce

LISTEN, LEARN, & EARN

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Advancing the Research Enterprise:

Establishing a New Standard Practice for Disseminating Clinical Trial Results to Study Volunteers

PEER REVIEWED | Zachary P. Hallinan, BA | Kenneth A. Getz, MBA

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Nearly 40% of the global public feels that clinical research volunteers are "experimental test subjects, not people," according to the 2013 *Perceptions & Insights Study* conducted by the Center for Information and Study on Clinical Research Participation (CISCRP) among 5,701 respondents.[1]

LEARNING OBJECTIVE
After reading this article, participants should be able to discuss benefits, challenges, and best practices of communicating the summary findings of clinical research studies to the study volunteers in lay language.

DISCLOSURES
Zachary P. Hallinan, BA: Nothing to Disclose
Kenneth A. Getz, MBA: Chairman and Director of CISCRP

Although there is widespread recognition that study volunteers contribute to the advancement of public health, there is no real sense that they are respected by the research community as true partners in the discovery of new medical treatments. To the extent this "guinea pig" image persists in the minds of the public, the clinical research enterprise will continue to struggle with the low levels of engagement that lead to the average study doubling in duration to meet enrollment targets.[2]

Investigative site staff and research sponsors can make substantial progress in overcoming this perception with relatively minor adjustments to end-of-study practices. This article discusses a program through which more than 20 major and mid-size pharmaceutical and biotechnology companies are currently educating and engaging study volunteers post-trial by systematically communicating the overall trial results in simple, everyday language, via a process that ensures communications are strictly nonpromotional and adds minimal burden on sponsor or site staff. Benefits, challenges, and best practices are covered, with supporting qualitative and quantitative data collected from patients and investigative sites over a series of program evaluations.

Need and Value of Communicating Trial Results to Study Volunteers

A 2008 literature review found that, across 15 studies, a median 90% of clinical research participants want to be told the results of their trial.[3] Yet globally, just 35% of volunteers receive any reports or updates on the results after finishing a study,[1] and the posting of aggregate results data on government-sponsored trial registries is currently intended to serve only the needs of clinical research professionals.[4] In a recent survey of 213 study volunteers, 97% wanted to know their trial's results; but when surveyed more than two months after aggregate results had been made available on the ClinicalTrials.gov registry, just 9% had been able to learn the results[5] even when, as one respondent wrote, they "repeatedly asked."

The effect of this lack of communication and transparency is that most study volunteers come to feel they are no longer valued by the research community after their active participation has ended.[6] This not only may significantly and dramatically reduce willingness to participate in future trials,[7] but also leads to most study volunteers, unless deeply self-motivated to share their experiences, choosing not to advocate for clinical research among other patients who are considering participation.[8]

The need for greater transparency to study volunteers is now widely recognized across the research enterprise. The 2013 Declaration of Helsinki states that "all medical research subjects should be given the option of being informed about the general outcome and results of the study."[9] In the summer of 2013, a joint statement was issued by the Pharmaceutical Research and Manufacturers of America and the European Federation of Pharmaceutical Industries and Associations, committing to "sharing results with patients who participate in clinical trials" as one of five Principles for Responsible Clinical Trial Data Sharing.[10]

Furthermore, a survey of Canadian research ethics board chairs found 95% support for returning study findings to research participants.[11] Preliminary findings of research in progress suggest similar levels of support among institutional review boards (IRBs) in the U.S.[12] Perhaps most supportive of all are investigative site staff, who cite an ethical obligation as well as likely benefits for the research enterprise such as improved volunteer trust and retention.[5]

Globally, 71% of study volunteers say the prospect of receiving the trial results was "very" or "somewhat" important in their decision to enroll, on par with factors such as "quality medical care" (85% indicate this is very/somewhat important) and the opportunity to "learn about my disease" (79%). Among study volunteers from South America and Asia-Pacific countries, the prospect of receiving trial results was rated the most important factor in their enrollment decision, above even quality medical care[1] (see Table 1). At the same time, most study volunteers (95%) have trial experiences that are positive enough they would consider participating in future trials.[1]

Because the best-educated members of the lay public are those who have participated in trials, and have become familiar with the professionalism and integrity of the research system, these former volunteers also have the potential to serve as the research enterprise's strongest ambassadors. One of the primary barriers is the current lack of a systematic and industrywide effort to facilitate volunteers' education and engagement in the research process after active trial participation has ended.

Any perception that the communications about results are promotional or provided out of sponsor self-interest risks undermining the primary benefits to the research enterprise: demonstrating respect and restoring trust.

Challenges and Best Practices in Post-Trial Communication to Study Volunteers

To help address this critical unmet need, the nonprofit CISCRP has, since 2009, been working with research sponsors such as Pfizer, Eli Lilly, Shire, and others to communicate trial results to their study volunteers in simple, easy-to-understand language. Although early adoption rates were slow, the number of sponsors communicating trial results to their volunteers has doubled each of the past two years. Program evaluations consisting of focus groups, interviews, and surveys have revealed enthusiastic response from patients, 91% of whom indicate satisfaction with the "language for laypersons" summaries, as well as demonstrating objective gains in understanding on pre/post evaluations.[5]

Investigative site staff have been no less enthusiastic. Since launching the program, CISCRP has interviewed and surveyed more than 50 investigators, study coordinators, and network-level research directors for their feedback. Of those, only one investigator felt that patients do not want to know their trial's results and should not be told, whereas all others indicated that there is a substantial need for a program to communicate trial results in lay language, and that they appreciated the opportunity to disseminate results to their patients.

TABLE 1. How important were the following factors in your choosing to participate in a clinical research study?

Percent rate "Somewhat/Very Important"		GENDER		REGION*			
	OVERALL	FEMALE	MALE	NA	SA	EU	APac
Quality medical care	85%	90%	79%	90%	55%	61%	58%
Access to medical professionals	83%	88%	78%	88%	57%	63%	57%
Learn about my disease	79%	83%	74%	84%	47%	55%	59%
Receive information about the results after the study has ended	71%	73%	69%	73%	68%	55%	59%
Receive regular updates about the research while I'm enrolled	68%	70%	66%	71%	59%	52%	57%
Feel part of a community	61%	65%	57%	62%	63%	57%	53%

Base: Have Participated (N=1,724)
**Regions: NA = North America; SA = South America; EU = Europe; APac = Asia-Pacific*
Source: CISCRP, 2013 Perceptions & Insights Study

One study coordinator wrote that, "In my 25 years of conducting clinical trials, I have never been able to let subjects know how the study turned out." Many interviewees echo this sentiment, adding that a program to communicate trial results to study volunteers has the further benefit of ensuring that site staff are informed of the results.

Despite strong positive responses and rapidly growing recognition of the need for post-trial communication and education of study volunteers, transparency to patients has not yet become standard practice. In hopes of seeing all research sponsors implement post-trial communication programs, we share here three critical considerations derived from our work with more than 20 sponsors. These considerations focus on challenges to be overcome as the research enterprise moves toward greater respect for and transparency to study volunteers who give the gift of their participation in clinical research.

Three Critical Considerations for Communication

1. Ensuring that communications to study volunteers are strictly nonpromotional

The Food and Drug Administration (FDA) Amendments Act of 2007 makes provisions for requiring that sponsors post to ClinicalTrials.gov a "summary of the clinical trial and its results that is written in nontechnical, understandable language for patients." As of late 2013, however, no final ruling on this provision has been made, and the delay appears to be related to the law's requirement that the U.S. Department of Health and Human Services first determine "that such types of summary can be included without being misleading or promotional."[13] This is not a concern to take lightly, not least because any perception that the communications about results are promotional or provided out of sponsor self-interest risks undermining the primary benefits to the research enterprise: demonstrating respect and restoring trust.

The process CISCRP has developed over the past four years is as follows: Sponsors provide summary study findings to CISCRP in technical format, such as the aggregate results posting prepared for ClinicalTrials.gov or the comparable format planned for the European registry.[14] CISCRP, uniquely positioned as an independent nonprofit, convenes an objective editorial panel including medical and consumer health communication experts, patient advocates, and specialists to "translate" the technical findings into a lay-language summary that presents the same information but in U.S.-equivalent sixth- to eighth-grade language. The sponsor's research staff then perform a final check that the lay language trial results summary accurately reflects the technical/scientific report, prior to CISCRP disseminating the lay summary in print and electronic formats to investigative sites, to share with study volunteers.

This approach creates multiple checks against communications becoming promotional, with the sponsor separated from patients by both investigative sites and a patient-focused third party with no vested interest in the study outcome.

2. Investigative site staff must be kept central to the process of disseminating results

Qualitative program evaluations have identified two major barriers to investigators being able to share trial results with their patients. First, investigative site staff report that sponsors do not consistently provide them with aggregate results. Second, results dissemination typically is not planned for in the study process; without support from the sponsor, sites do not have the resources to re-contact all patients a year or more after the study has closed.

At the same time, however, study coordinators and investigators consistently report that they must ultimately be responsible for any communications to their patients. This ensures patient privacy, and provides an opportunity to deepen the relationships developed between study volunteers and site staff over the course of a clinical trial.

Volunteers confirm that relationships with site staff are fundamental to a positive trial experience.[8] Site staff also note that there may be times when communications should not be sent to patients; one representative comment indicates, "We're so close with our patients…you know when it is appropriate to send and when it's not."[15]

As more sponsors begin regularly communicating trial results to their volunteers, it is critical that the central role of the investigative site be recognized and leveraged while minimizing any added burden on study staff. The CISCRP process accomplishes this by providing all patient materials to sites in mail-ready envelopes, so that sharing results with study volunteers can be as simple as adding an address and postage.

In certain cases, it may be appropriate to provide the lay language summary of results by e-mail, but volunteers report that receiving a printed, physical copy is important.[5] To this printed report, some investigative sites add further personalization, from a handwritten note to an evening event during which the investigator discusses the results with his or her patients using the written lay language report as a jumping-off point.

Even when staff resources do not allow for these additional steps, almost all sites are able to mail a printed report to their study volunteers.[5] In evaluations, site staff have estimated time commitments ranging from 30 minutes to two hours per study. Greater commitments come not when sites have high numbers of patients (even sites with 40 or more patients report half-hour time commitments), but when patient records have been moved offsite into archival storage.

3. Plan for results communication from the earliest point feasible

Many sponsors begin communicating trial results to study volunteers through pilot programs involving studies that have been or are soon to be completed. Though feasible on a pilot basis, our research and experience suggests that the ideal process plans for and integrates trial results communication from study initiation onward. This minimizes time commitments required of investigative site staff, who can hold patient contact information available until trial results are ready to disseminate, and ensures that the communications process is built into the study budget.

Although the cost to implement a clinical trial results communication initiative is low, it is often difficult for clinical teams to secure funding, as the initial budget is unplanned. This is perhaps the greatest upfront barrier to sponsors beginning a results-communication process.

FIGURE 1. CISCRP's Process for Communicating Trial Results to Study Volunteers

Making the commitment to communicate results from the start of the study also ensures the greatest benefits to study volunteers, sites, sponsors, and the research enterprise as a whole. Among other benefits, study volunteers are reassured that sponsors intend to be fully transparent, no matter the study outcome (and volunteers are clear that they want to know the results whether positive or negative[3]), helping to address widespread mistrust of the research enterprise.[6] The prospect of learning how the study contributed to the advancement of medical knowledge may also create greater engagement during the trial, helping to fulfill the altruistic motivations that are among the most important factors leading to the decision to enroll in a clinical research study.[1]

Engagement of study volunteers can be further strengthened with ongoing communication to bridge the gap between their last study visit and the time that trial results are ready to be shared[5] (see Figure 1). Ethics committees need to review the informed consent language and the "Thank You" communication described in Figure 1, both of which would be provided to patients actively participating in a clinical trial. In CISCRP experiences to date, ethics committees have typically indicated they would not be involved in reviewing the lay-language summary of trial results, which reflect publicly available information being provided to former study volunteers who are no longer enrolled in a clinical trial. In all cases, we recommend, and sites consistently appreciate, the sponsor planning for ethics review as early as possible in the communications process.

Conclusions and Next Steps for the Research Enterprise

There can be no doubt that the research enterprise is pushing toward greater transparency for the scientific community—from the U.S. Trial and Experimental Studies Transparency Act of 2012,[16] to the European Medicines Agency's plans to release trial data sets,[17] to calls for open data from the AllTrials Campaign and leading medical journals,[18, 19] as well as commitments by sponsors.[10, 20] As it happens, we cannot forget that translational research is possible only with the participation and engagement of study volunteers, and that we owe study volunteers not only our sincerest gratitude, but also the respect of ensuring that they are among the first to learn the results of their study.

Barriers still remain in ensuring that all volunteers are informed of the results of their clinical trial. In the U.S., without regulatory guidance there is no formal mechanism for IRBs to require a results communication plan of sponsors, despite the acknowledged ethical requirement.[9] While the Association for the Accreditation of Human Research Protection Programs' guidelines urge a results dissemination plan, there is no requirement that study volunteers be included.[21] Currently, the International Committee of Medical Journal Editors has no clear policy on the implications for scientific publication of sharing trial results with study volunteers,[22] and this lack of clarity may prevent results being shared or delay the process to such an extent that the results are no longer of relevance to volunteers. Perhaps most importantly, all sponsors—private and public—must make the commitment to study volunteers, integrating post-trial communication and education into the study planning process for each and every trial.

Translational research is possible only with the participation and engagement of study volunteers. We owe study volunteers not only our sincerest gratitude, but also the respect of ensuring that they are among the first to learn the results of their study.

More generally, post-trial communication must become part of the research enterprise's commitment to educate study volunteers at all stages of their trial experience. This starts with broad-based educational opportunities for the general public to learn about clinical research outside the pressures of deciding whether to participate.[23] It continues with an effective informed consent process and frequent communication over the course of the trial about study progress.[1] Further, the commitment must extend even beyond the time that trial results have been provided, with opportunities for patients to share their experiences and advocate for appropriate participation among others who are considering joining a clinical trial.

It is this virtuous cycle, engaging and educating volunteers who can share their knowledge and experience with future volunteers, that provides one of the best hopes for moving the research enterprise forward.

CISCRP research and experience suggest that the ideal process plans for and integrates trial results communication from study initiation onward.

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Increasing Provider Engagement in Clinical Research Starts with Research Awareness:

Leveraging Education and Technology to Improve Participation

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The advancement of current healthcare practices and knowledge requires continued clinical study enrollment and healthcare provider awareness of research opportunities. Bolstered by healthcare reform, meaningful use, and innovations in technology, healthcare research has potential for meaningful innovation and impact in the coming years.

LEARNING OBJECTIVE
After reading this article, participants should be able to describe the concept of research awareness, its impact on clinical research, and approaches to increasing research awareness among healthcare providers.

DISCLOSURES
Kathleen M. Aguilar, MPH; Candida Barlow, MSN, CTN, RN; Bonnie B. Dean, PhD, MPH; Kelly J. Ko, PhD: Nothing to Disclose

In fact, federal organizations and initiatives such as the Patient-Centered Outcomes Research Institute and Clinical and Translational Science Award Consortium were designed to facilitate research to improve healthcare delivery and outcomes. New tools such as Informatics for Integrating Biology and the Bedside (i2b2) allow researchers to have novel access to clinical data from electronic healthcare records (EHRs) and to better inform clinical study enrollment through cohort discovery.

Despite these initiatives and tools, clinical research continues to struggle with identifying and recruiting patients to participate. There must be greater engagement in research by institutions, healthcare providers, and patients for improvement through research.

Currently, less than 5% of the U.S. population participates in clinical trials each year.[1,2] As a result, approximately 85% of trials are delayed because of accrual challenges, and 30% never even enroll a single patient.[3] Furthermore, ethnic minorities, women, and older populations remain underrepresented in research studies, which limits the generalizability of most study-derived data to underrepresented populations.[2]

Increasing volunteers' involvement in clinical research requires overcoming challenges such as patient distrust, misunderstanding, or disinterest.[4,5] Recent evidence suggests that many patients not only recognize the value of research, but are willing to participate.[6–8]

One important factor may be the role of healthcare providers—especially physicians and nurses—who are either unaware of, uninterested in, or not connecting patients with clinical studies for which they may qualify. Thus, this article aims to examine research awareness and participation barriers among providers in medicine and nursing, their implications for study recruitment and retention, and approaches for overcoming them.

Healthcare Provider Engagement in Research

Providers are typically viewed as gatekeepers for clinical research, with studies relying on them to recruit and refer patients. Without providers, most patients would be unaware of the option to participate and unsure whether participation would be appropriate.[9] During the early evaluation phase, providers are the most likely to explain clinical trial participation to their patients, and may help patients overcome concerns about participating through establishing trusted relationships.[10,11]

This is true for providers actively participating in clinical research as well as those who do not participate, but who do refer patients. Furthermore, as research studies progress, providers also assist with clinical care, follow-up and retention, and

monitoring for adverse events or protocol violations. Even providers not participating in clinical research play a role in identifying adverse events and ensuring protocols are not violated. Thus, providers can be involved with research both directly or indirectly.

Despite their key role in the process, providers may hesitate to engage in research activities for various reasons.[12,13] Providers may have concerns about the safety and efficacy of the study, or research may be a burden on their workload, offer insufficient reimbursement, or be challenging to communicate to patients. Characteristics of research at their organization may also be barriers. For example, the research may be inefficient and disrupt workflows, or it may not be part of the organizational culture.

Last, and perhaps most importantly, a fundamental lack of research awareness may be the most prevalent reason for insufficient provider involvement. One survey found that 70% of patient respondents had never even discussed clinical research with their provider.[7] Likewise, in another survey of patients with cancer, 80% reported they did not consider participation because they were unaware that a clinical trial could be part of their care, and 40% did not understand the concept of a clinical trial.[8]

Why Research Awareness?

Research awareness refers to the extent to which providers at an organization are knowledgeable about ongoing clinical studies and understand how to recruit patients, address questions, and facilitate study protocols. In essence, having research awareness is the first step toward providers being directly or indirectly involved with research. Without research awareness, providers will not identify research opportunities with potential value for their patients, evaluate the appropriateness of studies for patients considering participation, or explain the risks and benefits of studies to them.

In addition to increasing patient recruitment for clinical studies, research awareness may improve health outcomes through access to novel treatment regimens not currently available to the general patient population. These therapies are often limited only to those enrolled in particular studies, and therefore restricted to patients whose providers are engaged in the research. In this regard, clinical research provides individual patients with access to trials that may improve their care and lead to a greater good for future patients.

Research awareness may also be important for patient safety. If providers are aware of ongoing research studies in which their patients are participating and are able to obtain the study protocol, their treatment decisions can improve patient safety and reduce protocol violations. For example, a provider with research awareness is less likely to prescribe treatment that is contraindicated with a study medication, and more likely to recognize a study-related adverse event.

The relationship between research awareness and provider engagement has not been extensively investigated in the literature, despite some available evidence suggesting an association. Recently, Somkin[14] performed a survey of medical oncologists' attitudes toward clinical trials and observed that awareness of trials was most strongly associated with respondents' willingness to enroll patients. Another study, comprised of physicians practicing in a Comprehensive Cancer Center network, found that 94.6% of primary care physicians, 84.1% of specialists, and 50% of oncologists rated lack of awareness or information about clinical trials as a top reason for not recruiting patients.[15] Taken together, poor recruitment rates contribute to higher costs and longer study durations.

Additional evidence suggests providers have a high interest in research, but are often unaware of study opportunities. Among 500 European physicians, Jones et al.[16] observed that 98% expressed a willingness to facilitate research for their patients with Alzheimer's disease, but only 19% were aware of local clinical trials.

Likewise, in Powell et al.'s[17] survey of physicians who had attended a training program aimed at increasing minority involvement in research,

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70.5% of physicians who responded were interested in participating in research. A lack of provider awareness was the most commonly cited barrier, reported by 43% of respondents. Moreover, this lack of awareness may be most significant for providers treating patients with chronic or severe conditions with few treatment options.

Even in fields like oncology, where clinical trial participation is relatively high, only a small proportion of oncology patients are enrolled in such studies.[18] For example, Zhang et al.[19] noted that although 67.6% of oncology providers believed that their patients would benefit from Phase I clinical trials, those with little or no understanding of cancer clinical trials were unwilling to recommend participation to their patients.

Insufficient research awareness may also contribute to low provider engagement in other ways, such as distrust of clinical trials, difficulty communicating research to patients, and an organizational culture that does not focus on research. For example, Ulrich[20] performed a survey of nurse practitioners and found that those who were comfortable discussing trials with patients were nearly five times more likely to believe in the value of clinical research.

Additionally, Howerton et al.[10] performed a literature review to assess provider-related barriers against minority enrollment in cancer clinical trials. Of the 18 articles reviewed, 14 included provider attitudes or perceptions toward research as obstacles for patient accrual, although only two studies specifically cited a lack of protocol availability and provider awareness. Taken together, these results suggest a relationship between providers' research knowledge, beliefs, and willingness to participate.

Increasing Awareness Through Education

Certain provider and organizational characteristics have been associated with greater trial participation—in particular, specialty type, teaching involvement, and cancer center affiliation.[21] These trends may be at least partially explained by deeper foundations of research education and experience in certain types of organizations and among certain kinds of providers, which in turn increase research awareness. Systematic approaches to increasing the saliency of research through provider training may improve engagement.

Research Awareness in Practice: A Case Study

A large Southern health system was engaged in approximately 150 active studies. Recognizing the value of clinical research, the organization's leadership wanted to explore approaches to expand their participation in research activities. A survey of providers was undertaken to assess awareness and opinions of the organization's potential for research. The survey was also intended as a benchmark for understanding the current state of research in the health system and requirements for its future expansion.

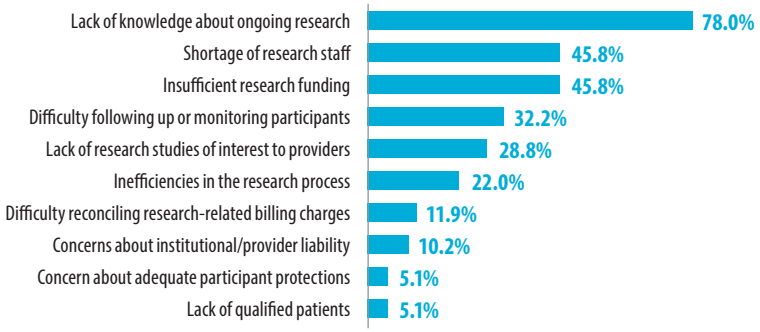
Results from the survey indicated that providers lacked knowledge about ongoing research. In total, 64 providers provided responses to the electronic survey (approximately 10%). Of the respondents, 70% rated the organization as performing less clinical research than similar institutions. Although this may have been an accurate representation of the then current state of research at the institution, perhaps it also indicated a lack of research awareness.

Our results suggest the latter, because 47% of respondents were unaware that any clinical trials or interventional studies were being conducted at the organization. Moreover, 62% were unsure whether their patients could be participating in clinical trials, and 68% did not know whom to contact even if they had a question about a study. Perhaps most importantly, lack of knowledge about ongoing research was rated as a significant barrier by 78% of respondents (see Figure 1).

Insufficient research awareness may have led to missed opportunities for clinical research at the organization. Although 95% of respondents did not believe lack of qualified patients would be a barrier, 77% said they never discussed potential clinical trials with their patients. Furthermore, 86% of respondents stated that they never talked to their patients about participation in clinical research, despite 95% rating clinical research as being beneficial.

Although this was a relatively small survey conducted at a single institution, these results highlight the significance of research awareness among providers for an organization's capacity to facilitate clinical research. Results from the research awareness survey were presented to the health system's executive board, which is now exploring education and technological interventions to improve awareness and promote research participation and knowledge.

FIGURE 1. Breakdown of Respondents' Ratings of Significant Challenges to Research at the Organization



Research education can begin during undergraduate, graduate, or residency programs.[12] During this time, providers can learn the fundamentals of research methodology and design, as well as develop a basic understanding of the research process.

Although some institutions may offer residents specific research rotations, this may not be an appropriate path for all providers, given the financial costs and time taken away from clinical experience.[22] Instead, offering educational opportunities such as research lectures, problem-based learning discussions, and mentorship may be sufficient to increase research involvement among students and residents.[8]

In general practice, continuing medical education can improve research awareness. Education and experience emphasizing research best practices, patient communication, and the importance of clinical studies for healthcare innovation would help increase research awareness among providers. For example, Sherwood et al.[23] reported that primary care providers who attend clinical trial education sessions were more likely to refer their patients to research. Similarly, Fink et al.[24] found that journal club participation increased research utilization among nurses. Furthermore, study sponsors and clinical research organizations may support ongoing learning activities through funding and content development.

Other electronic resources are available for providers who proactively want to find information about specific clinical trials or research opportunities. For example, one of the primary sources is the ClinicalTrials.gov website, which was established in 2000 by the National Library of Medicine at the National Institutes of Health (NIH) to be a repository of information about clinical studies.[25] Designed for patients, caregivers, providers, researchers, and the public, this website offers details such as study design, eligibility criteria, and investigators' contact information.

The NIH also hosts a site at www.nih.gov/health/clinicaltrials/providers/, which describes recommendations for how providers can become engaged in research and connect their patients with relevant opportunities.[26]

Increasing Awareness Through Technology

To supplement research education, technological approaches can also be used to increase provider exposure to clinical research opportunities. Through electronic screening and cohort discovery, providers and investigators can use data collected as part of clinical care to conduct automated screening of potential study participants.

Despite the costs associated with implementing technology aimed at research awareness, the worthwhile benefits to organizations and individual providers may include spurred innovation, increased revenue, and enhanced provider satisfaction.[27,28] In fact, with EHRs becoming more widely adopted, using electronic patient data to identify potential study participants has also become increasingly common.

Typically, research studies have relied on the provider's recollection of potential studies to bring awareness of opportunities to potential participants.[3] Given the multitude of studies being conducted and the variations across studies, relying solely on provider recall will likely result in missed research opportunities for participation. With electronic screening, providers can identify research opportunities relevant to their patients without having previous familiarity with the studies.[29,30]

At organizations with electronic screening solutions, study investigators or research coordinators enter the study-specific inclusion and exclusion criteria into a computer program that is integrated with the EHR. During a patient visit, the provider can initiate an algorithm that matches patient information from the record with study criteria. Alternatively, a study coordinator can electronically screen a patient population and send

Without research awareness, providers will not identify research opportunities with potential value for their patients, evaluate the appropriateness of studies for patients considering participation, or explain the risks and benefits of studies to them.

Education and experience emphasizing research best practices, patient communication, and the importance of clinical studies for healthcare innovation would help increase research awareness among providers.

automatic alerts to providers of potential participants. If the patient is suitable for a study, the provider can introduce the research or request that a study coordinator follow up. Electronic screening, therefore, can increase awareness of potential studies and eliminate the need for providers to know details about which study protocols are available.

Research technology can improve awareness by providing relevant patient alerts to providers. For example, a clinical trial management system (CTMS) may be configured to display whether a patient is participating in a trial whenever a provider accesses the healthcare record; providers can then consider this information when developing a treatment plan to ensure patient safety. This is particularly important for patients receiving experimental medications or therapies, to help avoid costly drug interactions, safety errors, or protocol violations.

Likewise, electronic alerts can be triggered to inform providers of study-related adverse events or protocol violations. A recent study involving physicians found that a clinical trial alert embedded in the EHR that triggered at the point of care was viewed as helpful, and that most physicians requested to receive similar alerts for other clinical scenarios.[18]

Unless prompted to this information during a patient visit—directly at the point of care—providers must rely on patient recall or chart notes for study information, both of which may be missed during a patient visit. Additionally, study personnel can directly enter protocol-related orders into the EHR, which facilitates alerts and hard stops to prevent safety errors and protocol deviations.

Technology also can help providers have a better understanding of ongoing research by increasing accessibility of study-related information, including documentation and investigator contact information. Lack of access to study information is commonly rated by providers as a key reason for not discussing clinical research with their patients.[31–33]

Before recommending a study to their patients, providers need sufficient knowledge to determine its appropriateness. Without a centralized electronic repository, however, accessing information about studies can be a burden. Providers may have to locate and review paper-based consent forms, study protocols, or other documents. If there are questions about the study, they must determine who to contact and how to reach that person. In contrast, through secure messaging services embedded in the EHR, technology can streamline the research communication process.

CTMSs and electronic repositories of study information may have different advantages for large academic medical centers, smaller community hospitals, and private practices, although every organization will face unique challenges. Larger facilities may be able to more easily leverage existing information technology (IT) infrastructure to implement tools with the potential to connect a sizable number of patients to research studies. This may allow organizations to reduce the staff burden of research, gain additional revenue, and participate in research networks. However, larger organizations may have more hurdles to overcome in order to deploy technology that meets the needs of multiple stakeholders within the organization.

Smaller community hospitals may have a less developed IT infrastructure, but benefit from the innovation, satisfaction, and revenue that research tools can provide. Additionally, at smaller institutions, physicians and researchers often work closely together, which may help to facilitate the adoption of this technology.

However, given IT requirements and costs, private practices may not be able to deploy full systems found at larger organizations, but can still greatly benefit from basic CTMSs and research tools, such as those for cohort discovery or understanding which patients are already participating in research. This technology may reduce the manual burden of chart searching and, potentially, raise revenue associated with trial participation, especially for private practices frequently participating in clinical trials.

Conclusions

Although several factors are associated with participation in clinical studies, much of the existing evidence assumes that providers are aware of potential research studies and know how to discuss these opportunities with their patients. Given their key role in the research process, lack of research awareness among providers likely has a significant effect on study recruitment and retention.

Increasing research awareness may help improve health outcomes and patient safety. Leveraging education and technology to improve research awareness will increase physician engagement. Future studies should more fully explore the lack of research awareness among providers and approaches for overcoming this barrier.

Despite the costs associated with implementing technology aimed at research awareness, the worthwhile benefits to organizations and individual providers may include spurred innovation, increased revenue, and enhanced provider satisfaction.

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HOME STUDY HS

Achieving Excellence Through Education and Training

OPEN BOOK TEST

This test expires on June 30, 2015

(original release date: 6/01/2014)

Moving from Compliance to Competency: A Harmonized Core Competency Framework for the Clinical Research Professional

1. In most countries, the minimal requirement to be a principal investigator (PI) is that one must document which of the following?

- **A.** Previous experience in conducting clinical research
- **B.** Professional certification in clinical research
- **C.** A valid medical license
- **D.** A doctoral degree

2. One can infer that education and training in the conduct of clinical research will result in which of the following?

- **A.** Increased regulatory compliance
- **B.** A reduced number of errors in case report forms
- **C.** Increased competency
- **D.** More rapid upward mobility within the profession

3. Which of the following applies to standardized job descriptions and educational requirements for roles within the clinical research enterprise?

- **A.** They are common throughout the pharmaceutical industry.
- **B.** They are required by ICH GCPs.
- **C.** They are more common in Europe than in the United States.
- **D.** They would be valuable tools for assessing the level of competency.

4. The Joint Task Force for Clinical Trial Competency (JTF) has worked toward which of the following efforts?

- **A.** Creating a list of required competencies for all clinical research professionals
- **B.** Defining the knowledge necessary to function as a clinical research associate (CRA) or clinical research coordinator (CRC)
- **C.** Attempting to align and harmonize previous efforts to define the competencies required for the conduct of clinical research
- **D.** Beginning the process of accrediting academic programs in clinical research

5. How does the article define a competency domain?

- **A.** A broad category of knowledge, skills, and attitudes necessary to function within the field of clinical research
- **B.** A region of the country where there is a concentration of academic programs and training companies
- **C.** A specific skill necessary to function within the clinical research enterprise
- **D.** A mechanism to define the level of knowledge or experience necessary to qualify for professional certification

6. Which is true about the core competency statements in the JTF Framework?

- **A.** They suggest that everyone who participates in the clinical research enterprise must be competent.
- **B.** They were developed by harmonizing the many relevant statements already published by other groups.
- **C.** They apply only to Federal Drug Administration (FDA)-regulated clinical research activity.
- **D.** They are each applicable to several competency domains.

7. One potential outcome of developing the Core Competency Framework is that it will standardize which of the following?

- **A.** Education and training necessary to be a PI
- **B.** Education and training necessary to be a CRC
- **C.** Education and training necessary to be a CRA
- **D.** Content of educational programs that contribute to the development of clinical research professionals

8. One of the potential benefits of defining the competencies required to conduct clinical research involves which of the following?

- **A.** Reducing redundant education and training programs for clinical trial staff
- **B.** Enhancing the level of quality of clinical trials conducted in developing countries
- **C.** Increasing the ethical awareness of clinical research professionals
- **D.** Decreasing the number of adverse events that occur in clinical trials

9. According to this article, the JTF has proposed which of the following?

- **A.** All clinical research personnel attain the highest level of competency in each domain
- **B.** All clinical research personnel are to be tested for competency
- **C.** The Competency Framework be adopted and maintained within ICH GCPs
- **D.** The Competency Framework replace the current ICH GCPs

10. Which of the following best describes the mission of the JTF?

- **A.** To bridge the gap between what to do and when to do it
- **B.** To bridge the gap between what to do and how to do it
- **C.** To bridge the gap between why it should be done and how to do it
- **D.** To bridge the gap between what should be done and who does it

Advancing the Research Enterprise: Establishing a New Standard Practice for Disseminating Clinical Trial Results to Study Volunteers

11. What do the authors suggest happens when study volunteers are NOT told the results of their study?

- **A.** Research sponsors may conduct unnecessary clinical trials in the future.
- **B.** Study volunteers become more willing to participate in future studies.
- **C.** Study volunteers are able to find the results on their own through ClinicalTrials.gov.
- **D.** Study volunteers come to feel they are not valued by the research community.

12. Which of the following best describes what is in the 2013 Declaration of Helsinki regarding communication of study results?

- **A.** All study volunteers must be informed about the study results, whether they want to know or not.
- **B.** All study volunteers should be given the option of being informed about the study results.
- **C.** Physicians should use their best judgment to decide whether or not to disclose the results to the study volunteers.
- **D.** The results of the study should never be shared with the study volunteers, as this may cause undue psychological harm.

13. Which of the following did the article identify as factors that the majority of study volunteers considered important in their decision to participate in a clinical trial?

1. Speaking with an IRB representative
2. Receiving information about the study results
3. Receiving quality medical care
4. Learning about their disease

- **A.** 1, 2, and 3 only
- **B.** 1, 2, and 4 only
- **C.** 1, 3, and 4 only
- **D.** 2, 3, and 4 only

14. Which of the following best describes research cited in this article?

- **A.** Most study volunteers want to be informed of the overall study results, and most investigative site staff want to provide this information.
- **B.** Most investigative site staff want to inform study volunteers of the overall study results, but most study volunteers do not want to know.
- **C.** Most study volunteers want to be informed of the overall study results, but most investigative site staff do not think it is appropriate to provide this information.
- **D.** Neither study volunteers nor investigative site staff believe that volunteers should be informed of the overall study results.

Find the most current online test at **www.acrpnet.org/homestudy**, including any revisions made after publication of this issue of *Clinical Researcher*.

15. Which of the following does the article recommend to be best practices for implementing a program to communicate overall trial results to study volunteers?

1. Implement systems to ensure communications to volunteers are strictly nonpromotional.
2. Disseminate results only in printed formats to minimize access by unauthorized parties.
3. Keep investigative site staff central to the process of disseminating results.
4. Plan for communication of results as early as possible in the clinical trial process.

A. 1, 2, and 3 only **C.** 1, 3, and 4 only
B. 1, 2, and 4 only **D.** 2, 3, and 4 only

16. Which of the following has been identified as a barrier to investigative sites informing study volunteers of the overall study results?

A. Investigative sites report that research sponsors do not consistently provide aggregate results after studies conclude.
B. Many institutional review boards (IRBs) currently prohibit the dissemination of overall study results to study volunteers.
C. The FDA Amendments Act of 2007 currently prohibits the dissemination of overall study results to study volunteers.
D. The HIPAA Privacy Rule prohibits investigative sites from contacting study volunteers after the end of the study.

17. In the recommended results-communication process described in Figure 1, when should study volunteers FIRST be informed that they will receive a summary of the study results?

A. During the initial informed consent discussion
B. When it is clear the trial will not be terminated due to low enrollment
C. After the last patient visit but prior to database lock
D. After the study is publicized by a major news outlet

18. Which of the following are identified as potential benefits of regularly communicating overall trial results to study volunteers?

1. Better health outcomes and fewer side effects for the study volunteers
2. Deepening the relationships developed between study volunteers and site staff over the course of a clinical trial
3. Addressing widespread mistrust of the research enterprise
4. Helping fulfill study volunteers' altruistic motivations for participation in clinical research

A. 1, 2, and 3 only **C.** 1, 3, and 4 only
B. 1, 2, and 4 only **D.** 2, 3, and 4 only

19. Which of the following best describes the current role of IRBs in communicating trial results to study volunteers in the United States?

A. U.S. federal regulations require IRB approval before communicating trial results to study volunteers in any way.
B. U.S. federal regulations require IRB acknowledgment but not approval before communicating trial results to study volunteers in any way.
C. Despite ethical grounds, IRBs in the U.S. have no formal mechanism for requiring a results communication plan from research sponsors.
D. IRBs in the U.S. have clear authority to require a results communication plan from research sponsors.

20. Which of the following best summarizes the International Committee of Medical Journal Editors (ICMJE) policy on sharing trial results with study volunteers?

A. Providing a summary of results to study volunteers will not affect eligibility for scientific publication.
B. There is currently no explicit policy on the implication for scientific publication of sharing trial results with study volunteers.
C. Providing a summary of results to study volunteers will always make the findings ineligible for scientific publication.
D. Providing a summary of results to study volunteers will make the findings ineligible for scientific publication only in the case of oncology trials.

Increasing Provider Engagement in Clinical Research Starts with Research Awareness: Leveraging Education and Technology to Improve Participation

21. The article cites evidence that estimates what percentage of the U.S. population participates in clinical trials annually?

A. Less than 1% **C.** Approximately 10%
B. Less than 5% **D.** More than 25%

22. In the article, research awareness is defined as which of the following?

1. Having knowledge of ongoing clinical studies
2. Understanding how to recruit patients
3. Acknowledging conflicts of interest and study sponsorship
4. Being able to address questions about the study protocol

A. 1, 2, and 3 only **C.** 1, 3, and 4 only
B. 1, 2, and 4 only **D.** 2, 3, and 4 only

23. According to the article, why might research awareness be particularly important for healthcare providers treating patients with few treatment options?

A. Novel therapies may be limited to patients enrolled in specific trials.
B. A large proportion of these patients are enrolled in clinical research.
C. More grant funding is available for studies of these populations.
D. Publication opportunities are more likely for these types of trials.

24. Which of the following is an example of how research awareness may also be important for patient safety?

A. Healthcare providers may be more likely to encourage patients to take medications as prescribed.
B. Healthcare providers may be more likely to share care plans with multidisciplinary teams.
C. Healthcare providers may be more likely to avoid prescribing treatment contraindicated with a study medication.
D. Healthcare providers may be more likely to follow evidence-based practices.

25. According to the case study, healthcare providers rated which of the following as the most significant challenge to research at their organization?

A. Lack of qualified patients
B. Shortage of research staff
C. Lack of research studies of interest to providers
D. Lack of knowledge about ongoing research

26. Which of the following healthcare provider and organizational characteristics have been associated with an increased involvement in clinical research?

1. Geographic location
2. Specialty type
3. Teaching involvement
4. Cancer center affiliation

A. 1, 2, and 3 only **C.** 1, 3, and 4 only
B. 1, 2, and 4 only **D.** 2, 3, and 4 only

27. The article describes which of the following approaches to increasing research awareness through education?

1. Undergraduate, graduate, and residency programs and mentorship
2. Continuing medical education coursework and journal clubs
3. Mandatory institutional-sponsored research tutoring sessions
4. Electronic repositories of information about research opportunities

A. 1, 2, and 3 only **C.** 1, 3, and 4 only
B. 1, 2, and 4 only **D.** 2, 3, and 4 only

28. How can electronic screening decrease the research participation burden on healthcare providers?

1. Reduce the need for providers to know inclusion and exclusion details of study protocols.
2. Send automatic alerts to providers when their patients qualify for research studies.
3. Enroll patients automatically if they qualify for a research study.
4. Send automatic alerts to providers when new study protocols are available.

A. 1 and 2 only **C.** 2 and 3 only
B. 1 and 4 only **D.** 3 and 4 only

29. Which of the following is mentioned as a benefit for storing study-related documentation, such as consent forms and study protocols, in a centralized electronic repository?

A. Documents cannot be modified
B. Public availability of study information
C. Increased accessibility of study information
D. Retention of only essential documents

30. Which of the following ways can the electronic healthcare record be leveraged as a tool to increase research awareness among healthcare providers?

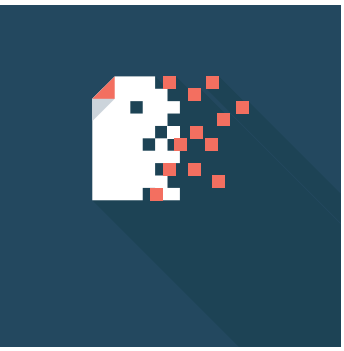
1. Electronic screening algorithms can use the underlying clinical data to automatically identify potential study participants.
2. Electronic prompts can offer guidance to providers needing assistance with patient questions about the studies.
3. Automatic alerts can help providers know whether a patient is on a trial, experiencing a study-related adverse event, or has violated the study protocol.
4. Accessibility of study-related information can be increased by storing documentation in an electronic repository and enabling secure messaging with research personnel.

A. 1, 2, and 3 only **C.** 1, 3, and 4 only
B. 1, 2, and 4 only **D.** 2, 3, and 4 only

AMC ROUNDTABLE

Paula Smailes, RN, MSN, CCRC, CCRP | Wendy Walters, MS, RD

The Many Considerations for Researcher Education on Electronic Medical Records



The electronic medical record (EMR) has proven to be one of the biggest innovations in recent times for the implementation of healthcare services. The adoption of EMR systems by healthcare facilities is strongly supported and incentivized by the U.S. federal government via the Health Information Technology for Economic and Clinical Health (HITECH) Act.

Facilities that currently use this technology know firsthand the ease of documentation, communication, billing, scheduling, and procedure ordering across multidisciplinary teams. Researchers at academic medical centers (AMCs) can be included in the multidisciplinary teams that can benefit from its use.

However, researchers have certain challenges related to EMRs based on the nature of their usage and workflows. This proves to be complicated for those in information technology (IT) who are responsible for providing security, access, and training for clinical research. These items are not mutually exclusive, and the type of training is based on the security vetting and access received. The research enterprise at AMCs complicates the situation even more, as research practices differ vastly across departments, settings, and therapeutic areas.

To ensure successful outcomes for researchers and the electronic records, there needs to be an IT infrastructure to support them. Such infrastructure may include builders, project managers, research billing, and trainers. The ultimate goal is standardization with a balance between operations, workflows, implementation, and optimization of the system. From the training perspective, the task can be daunting for many reasons.

To ensure successful outcomes for researchers and the electronic records, there needs to be an IT infrastructure to support them.

Roles

Research training should not be a one-size-fits-all endeavor. Research roles can be quite diverse, including assistants, associates, coordinators, nurses, investigators, schedulers, and billing staff. Although usage could overlap to some degree, their inherent differences may require individualized training based on role. For example, a research nurse will have more responsibilities than a research coordinator, and these differences need to be addressed in training.

Security Access

Access to the EMR system can allow a researcher exposure to millions of records. For this reason, those who gain access must meet specific security clearance.

Research considerations are based on what end-users will be doing in the electronic record, which, in turn, will determine what training is needed. This ties in to how access to and usage of EMRs has been explained in the end-users' application to the institutional review board (IRB) for conducting a study that would benefit from the availability of an EMR system. A determination will need to be made as to what the researcher's scope of access will entail, such as view-only, documentation, billing, and scheduling. There may also be a specific access for monitors and auditors, in addition to contract research employees.

Setting

In an AMC, research can be in either an inpatient or outpatient setting. Inpatient functionality of the electronic record is very different from that in ambulatory cases, and departmental differences also need consideration.

Clinical research workflows for cancer research may be quite different from workflows for endocrinology. These differences affect how the EMR is used, and the needs of the end-user. Researchers often look for specific functionality when they document their data, and all they need to do is change the department into which they are logged.

Documentation policies can help to guide researchers on what should and should not be placed in the record; these need to be determined at the institutional level. Training, in turn, should incorporate these policies.

Protocol Differences

Pharmaceutical studies may have a different type of usage than National Institutes of Health–sponsored research. For example, pharmaceutical studies that use a central lab obviously will not need to order labs in the electronic record, because they may be shipping out their specimens.

For studies that need to have blinded study staff, the use of the electronic record may not be an option, because there is no way to keep information blinded once entered into the system. Some AMCs use an electronic patient portal, where lab results are automatically posted. Blinding patients from results would be an issue, and another reason that perhaps the study should not be documented in the electronic record.

These decisions need to be made at the study level, and would be difficult for a governing authority to dictate.

Documentation Policies

Documentation policies can help to guide researchers on what should and should not be placed in the record; these need to be determined at the institutional level. Training, in turn, should incorporate these policies. One policy to consider is that there should be no documentation of research activity without a person's informed consent for research.

Although the IRB may not dictate how to specifically document in the electronic record, researchers do need to be cognizant on its use for recruitment purposes. Recruitment of participants using the electronic record must be approved by the IRB through a full or partial waiver of the Health Insurance Portability and Accountability Act.

Trainers specific to research need to know what institutional and regulatory policies dictate use of the EMR system when teaching research staff its use.

Instructional Design

Some institutions require new research staff to learn the foundations of EMRs for research in order to receive access to the system. Classroom training may be the most traditional method for research end-users.

The use of eLearnings, in which end-users can take the coursework electronically at their leisure instead of being dictated by scheduled offerings, may be beneficial. Researchers and their support staff are inherently busy, and this provides a convenient method for them to meet required training. Tipsheets can also be developed that take end-users step-by-step through new functionality.

Optimization sessions, where IT trainers meet one-on-one with end-users to ensure that they are using the system to its full capacity, are very useful. Researchers may believe that they need specific IT builds for their studies, when all they need is to know how the system works to maximize their use of existing functionality.

Classroom learning may be overwhelming for some users, because a lot of information is delivered at one time. Classroom settings may also prove challenging for those who have English as a second language, and who may thrive instead in a one-on-one format.

Another consideration involves adult learning methodologies; multiple methods can be used for roles so that the education is not more than it needs to be or too little. Ideally, there will be the right fit for each end-user; this can be challenging, yet it is an important consideration, as each person comes with his or her own expertise.

Training in EMR-related matters for researchers is no small topic. Like most areas of IT, research is constantly changing, and trainers must keep researchers abreast of the changes that are coming so they can stay current and use the system optimally.

Not only is technology evolving, so is the way teaching is delivered. Although traditional classroom settings have value, other methods such as webinars and e-Learnings have increased appeal. For busy AMC researchers, these flexible formats for EMR training can be beneficial.

Conclusion

There is a significant amount of planning that happens behind the scenes in IT to make sure that researchers can easily and efficiently conduct their studies. With the proper training, researchers will know how to recruit, document, run reports, schedule, and reconcile research billing work queues. Although becoming savvy with technology may be initially overwhelming, users quickly learn how their workflows can be optimized and simplified, thanks to the EMR system.

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Investigator Training and Education for Clinical Trials:

Current Developments within the European Union

PEER REVIEWED | Norbert Clemens, MD, PhD, CPI

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Clinical trials with pharmaceuticals and medical devices have been and will continue to be an area of discussion for all of the different stakeholders involved (regulators, captains of industry, patients, healthcare professionals) within the public. The requirements for protecting the rights, safety, and well-being of study participants are consequently focusing much attention on ethical considerations, compliance with privacy protection, and comparable regulations.

In addition, the environment of scientific and ethical consensus represented by the recent revision of the Declaration of Helsinki, introduction of pertinent new regulations in various nations, and the upcoming "upgrade" of the Clinical Trials Directive 2001/20/EC to a Regulation for the European Union (EU) is changing over time. One of the biggest challenges is therefore the transfer of the requirements into practical application through appropriate training and the according oversight of site and investigator qualifications by bodies like independent ethics committees (IECs).

This article will provide insight into current developments from a European perspective with 28 EU member states contributing to a certain level of complexity and divergence.

Regulatory Framework in the EU

Requirements for the conduct of clinical trials in the EU are provided in "Directive 2001/20/EC of the European Parliament and of the Council of April 2001 on the approximation of the laws, regulations, and administrative provisions of the member states relating to the implementation of good clinical practice (GCP) in the conduct of clinical trials on medicinal products for human use."[1] In this context, "medicinal products" are pharmaceuticals.

Directive 2001/20/EC had to be implemented into national legislation by all EU member states by mid-2004, and was adopted with the following objectives:

- harmonizing the EU regulatory environment for clinical research,
- improving the protection of participants,
- optimizing the use of safety information, and
- ensuring the credibility of data through a strengthened responsibility of the sponsors and harmonized trial authorization procedures for member states.

The Clinical Trials Directive's objectives were transposed into divergent national legislations through a process whose results partly missed the overall effort's goal of harmonizing clinical trial conduct and left multinational trials more difficult to perform than many had hoped.

Within the European Seventh Framework Programme (this is a €10 billion budget over five years to boost research and innovation), in 2008 a project was designed to measure the effect of the current EU legislation, analyzing its direct and indirect consequences. The project title was

"Impact on Clinical Research of European Legislation" (ICREL).[2] According to the final report, the 27 European member states released a total of 122 national legislations, and the expectation would have been not to exceed 27 national transformations of the Clinical Trials Directive.

In an attempt to achieve the same quality standards, almost similar procedures for all types of clinical trials with medicinal products are required—from registration trials with innovative treatments to trials comparing treatment strategies using marketed drugs and minimally invasive trials. Small- and medium-sized entities and academic institutions have especially to face major difficulties in fulfilling their sponsor responsibilities.

The outcome of ICREL raised massive concerns in terms of its effects on the competitiveness and attractiveness of the EU for clinical research.

Current Training Requirements in the EU

All parties involved in organizing and supervising clinical research agree that investigators need adequate training to carry out their duties, but the current qualification standards for investigators are generally vague and vary widely among EU countries. Only in Hungary, Lithuania, Sweden, Switzerland, and the United Kingdom is a certificate in GCP a minimum regulatory requirement to participate in clinical trials.

In some EU countries, like Germany and Italy, IECs expect to see a GCP certificate as a demonstration of investigator suitability. However, training over one or two days in GCP does not enable physicians to comprehend thoroughly their role in protecting trial participants and to generate quality data in an efficient way in all types of studies. Most IECs in Europe are satisfied with a *curriculum vitae* documenting clinical credentials in the respective therapeutic area.

The Clinical Trials Directive's objectives were transposed into divergent national legislations through a process whose results partly missed the overall effort's goal of harmonizing clinical trial conduct and left multinational trials more difficult to perform than many had hoped.

IECs review and evaluate the qualification of sites and site personnel. Throughout the EU member states, the number of IECs differs substantially, that is, from one to several hundred IECs per country.[2] Interestingly, there is no formal requirement for initial and ongoing training and education for IEC members across Europe.

Basic training is necessary for IEC members with regard to the ethics, laws, and methods of clinical research, and the current standard operating procedures of specific IECs. However, IEC members are selected mainly according their expertise in a certain field, such as nursing, law, or medicine. Other qualifications regarding clinical research are neither required nor taught. Thus, there are, in practice, only rudimentary requirements for training in the individual EU member states.

Current Developments

This situation has necessitated the development of a strategy for investigator training in Europe that

- is able to enhance the efficiency and reliability of investigator activities;
- follows a syllabus that covers the full spectrum of investigator activities, not just the GCP basics;
- is adapted to investigators' respective roles and responsibilities in a clinical trial;
- ensures demonstration of achieved learning outcomes; and
- can be applied in all EU member states.

This strategy has been proposed in a position paper published by two major initiatives, PharmaTrain and the European Clinical Research Infrastructures Network (ECRIN).[4] The main objective of the PharmaTrain project is to harmonize, build, and implement modular Masters-level programs in pharmaceutical medicine(s) development.

The proposed EU Clinical Trials Regulation aims at harmonizing the rules for the conduct of clinical trials in the EU, and also the acceptability throughout the Union of data generated in clinical trials.

ECRIN is a not-for-profit infrastructure supporting multinational clinical research projects in Europe.

The position paper references other international activities to increase investigator competence, such as the Organization for Economic Cooperation and Development,[5] the Academy of Physicians in Clinical Research,[6] and the Alliance for Clinical Research Excellence and Safety (ACRES)[7] initiative. The main goal of the proposal is the establishment of a European investigator training infrastructure leading to a clinical investigator certificate.[8]

Course materials tied to the PharmaTrain/ECRIN initiative delineate different competency levels for clinical researchers:

Level 1: Competency expected for members of the investigative team who are involved in the conduct of a trial's clinical operations, such as a sub-investigator.

Level 2: Competency expected for an investigator who is responsible for the organization and conduct of the study.

Level 3: Competency expected for an investigator who takes the initiative to launch a study and is actively involved in its design (sponsor-investigator).

After successful completion of the courses, the certificates will mention the level of competence and all nationally required information.

Outlook

Based on the ICREL report, the EU Commission prepared a proposal for a Regulation on Clinical Trials on Medicinal Products for Human Use (repealing Directive 2001/20/EC).[9] Adopted Regulations are immediate effective law in all EU member states without any national divergence (e.g., identical legislation in all EU member states), and this proposal has been formally ratified by the European Parliament and the Council of Ministers as of April 2, 2014, and will come into effect in mid-2016.

The proposed EU Clinical Trials Regulation aims at harmonizing the rules for the conduct of clinical trials in the EU, and also the acceptability throughout the Union of data generated in clinical trials. It should set high standards for the quality and safety of medicinal products by ensuring that the data generated in clinical trials are reliable and robust; but some may wonder if this includes clear training requirements.

Concerning investigator and site staff training and education, the proposed Regulation states the following:

Article 46—Suitability of individuals involved in conducting the clinical trial

The investigator shall be a medical doctor as defined in national law, or a person following a profession which is recognized in the Member State concerned as qualifying for an investigator because of the necessary scientific knowledge and experience in patient care.

Other individuals involved in conducting a clinical trial shall be suitably qualified by education, training and experience to perform their tasks.

M. SUITABILITY OF THE INVESTIGATOR (INFORMATION PER MEMBER STATE CONCERNED)

57. Description of the qualification of the principal investigators in a current *curriculum vitae* and other relevant documents shall be submitted. Any previous training in the principles of GCP or experience obtained from work with clinical trials and patient care shall be described.

As a result, the success of all efforts in the EU to harmonize training and qualification of investigators and site personnel will still depend on the voluntary cooperation and involvement of investigators, sponsors, IECs, and national regulatory authorities.

Therefore, initiatives such as that launched by PharmaTrain/ECRIN should join forces with global activities and existing certifications such as the Certified Physician Investigator (CPI®) from the Academy of Clinical Research Professionals, ACRES, and TransCelerate Biopharma Inc. (launched in September 2012 to advance innovation in research and development [R&D], identify and solve common R&D challenges, and further improve patient safety) to standardize the qualification requirements and to reduce time and costs of trainings.

The success of all efforts in the EU to harmonize training and qualification of investigators and site personnel will still depend on the voluntary cooperation and involvement of investigators, sponsors, IECs, and national regulatory authorities.

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From academia to biotechnology firms and everything in between, I have been fortunate to serve in many capacities throughout my 30-year career in clinical research.

An Interview with Linda Strause, PhD

This month's column focuses on the illustrious career of Linda Strause, PhD, who shares her insights on clinical research from a 360-degree perspective, having held numerous roles over the last 30-plus years.

Q: How did you first become interested in clinical research, and can you describe a little bit about the path you took to get involved with your clinical research career?

A: I started my career as an investigator at the University of California, San Diego (UCSD), doing osteoporosis research, beginning with animals and eventually transitioning into human research. Working as a post-doc in a biochemistry laboratory, we were exploring the role that trace minerals (manganese, zinc, and copper) had on bone health. I was eventually approached with a job offer from the contract research organization (CRO) Quintiles, which had been awarded a clinical trial for an osteoporosis project. I accepted and became the global clinical project advisor for that project.

Q: Can you tell us a bit more about the different types of roles you've held over the years?

A: My experience spans 360 degrees, having worked at the research site as an investigator, at a global CRO as a clinical project advisor, at a site network as a vice president, and at various sponsor companies in a variety of roles. In addition, I served as chair of the institutional review board (IRB) for San Diego Hospice for 15 years and consulted for many biotechnology companies. I still maintain a faculty appointment at UCSD, where I teach "Introduction to Human Nutrition." So, from academia to biotechnology firms and everything in between, I have been fortunate to serve in many capacities throughout my 30-year career in clinical research.

The protection of human subjects who participate in clinical trials will continue to evolve, especially with the increase in personalized, targeted therapies.

Q: When did you first get involved with ACRP, and what type of benefits have you reaped from being a member?

A: I was invited by a colleague to chair what was originally called the IRB Forum for ACRP. I changed this to the Ethics Committee, and went on to be a member on the Editorial Advisory Board for *Clinical Researcher*'s predecessor publication, *The Monitor*, chair of the Communication Committee, and chair of the Regulatory Affairs Committee. In addition, I served two terms on the Association Board of Trustees. I have also contributed as an author for *The Monitor* and as a speaker at many conferences, including ACRP's Global Conference. I was honored with the Top Speaker of the Year award for the ACRP 2013 Global Conference.

Q: Since your career has spanned many years and you have no doubt seen many changes, what is the most significant change (or top changes) you have seen? How has this affected the industry, either positively or negatively?

A: First, no matter what the changes, ethics remains highest in priority. The protection of human subjects who participate in clinical trials will continue to evolve, especially with the increase in personalized, targeted therapies.

Technology has been another area of huge change, particularly with the use of electronic data capture systems, which has fundamentally changed how we collect data. Data really are the "currency" of clinical trials.

There has also been a trend toward increased regulatory oversight, including, but not limited to, the Health Insurance Portability and Accountability Act, the European Union Clinical Trials Directive, privacy, financial disclosure, and, most recently, risk-based monitoring (RBM) guidelines. From my perspective, some of this oversight has had no impact other than to increase workloads (e.g., financial disclosure requirements), whereas others (e.g., RBM) will prove to streamline the clinical operation process.

Q: What advice do you have for clinical research professionals, in terms of how to advance their careers?

A: Stay informed and active in the clinical research environment, and interact regularly with colleagues. Push yourself to make career moves that will further your education and continue networking.

I like to say that it sometimes benefits you to "move up and out." Volunteer within our industry as well as with other organizations, whether on an editorial or advisory board for a journal or with another organization. For example, I am a member of the steering committee for the Southern California Women in Bio (WIB) Chapter. WIB is a national organization that promotes women in the life sciences. As I said, I also speak at numerous events, such as the Orange County Regulatory Affairs conferences, as well as for ACRP chapters and sponsor organizations. It keeps me on top of my field and provides great networking opportunities.

Q: As you think about the future generation of clinical research professionals, what three "lessons learned" would you like to share?

A: First, stay informed of the changing climate in clinical research from regulatory oversight to novel investigational agents.

Second, don't be afraid to make a decision! Just make sure you evaluate the effects of your decision and be nimble enough to change as appropriate.

Finally, remember that "it is more important to be respected than to be liked."

Q: Do you have any closing thoughts you would like to share?

A: I believe that the clinical research profession offers exciting opportunities to learn, grow, and make a difference whether you are in clinical, regulatory, technology, contracts, finances, quality assurance, or any other area of this industry.

ACRP appreciates your taking the time to discuss the myriad ways that one can find a challenging and rewarding career in clinical research. There's no limit to learning and growing, and it's a matter of taking advantage of the many opportunities that present themselves, as you have done.

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Research Education and Beyond:

A Foundation for Conducting High-Quality Research

PEER REVIEWED | Teri Lyn Crumb, BSN, RN, CCRC | Alison Dutkiewicz, BSN, RN, CCRN | Yvonne M. Edgerly, BSN, RN | Kimberly G. Mohr, BSN, RN, CCRC | Marianne M. Morrissey, BSN, RN

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Research staff education and training are key components of a research program. Everyone involved in clinical research must acquire a base knowledge and remain current on the regulations that are essential in the protection of human subjects involved in research. Over the last decade, institutional review boards (IRBs) have placed many new requirements on researchers, stemming from increased regulatory oversight and expectations from federal agencies and accrediting bodies.[1] Sites have an ethical obligation to support clinical researchers and equally to protect human subjects in research; to this end, training and continued education are necessary to conduct high-quality research.

Background

As a community-based teaching hospital system, Spectrum Health had a small but growing clinical research department in the 1990s. Research teams were acutely aware of the national reports of improper conduct of clinical research,[2] and discussed the need for more education of research staff. In 2003, the new regulations in the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule prompted additional education and policy changes throughout the system and had a significant impact on human subject health research.[3]

HIPAA increased the need for clinical research staff to be a resource to researchers and to assist with continued research activities. Growth on research teams in terms of new nurses, coordinators, and assistants, coupled with work toward accreditation from the Association for the Accreditation of Human Research Protection Programs for the site, led to the development of a formal education program to train new research staff in research regulations.

Because research staff typically were not hired with extensive research experience, the sites needed to provide the training and ongoing education to support the clinical trial activities.[4] As noted in a reference book for research coordinators, "[I]t is essential for (the clinical research coordinator [CRC]) to be aware of, and understand, all of the rules and regulations that apply in [his or her] region.... Education and training are the first tools that CRCs should be given for their clinical research toolbox."[5] As part of the education program at Spectrum Health, an education course, called Research 100, became the fundamental training program for the clinical research staff.

Research 100 Curriculum

Research 100 is a series of classes developed by the research department educator and other staff members, focused on giving new research staff an overview of clinical research and regulatory guidelines, as well as institution-specific policies and procedures. New clinical research staff employees are required to attend unless they can demonstrate competency in the areas covered by the curriculum.

TABLE 1. Topics Covered in the Research Courses

Curriculum	Research 100	Continuing Education	Research 200
Overview of the CRC and PI roles	X		
Good clinical practice	X		
Protocols and investigator brochures	X		
Informed consent process	X		
Study start-up activities (IRB submission, study documentation, study management, monitoring visits, and study subject management)	X		
Writing research protocols		X	
Recruitment and retention strategies		X	
IRB regulations, compliance, and ethics		X	
Statistical design		X	
Grant proposal development		X	
Research ethics		X	
Audits			X
Inspections			X
Continued quality assurance			X

The classes are part of the orientation process within the department and are scheduled during normal working hours. The original course content was based on research textbooks and federal and state regulations. Over the past several years, however, the content has been developed and refined, with the core topics continuing to focus on research fundamentals and the needs of inexperienced clinical research staff.

The goals of Research 100 are to provide staff with the core knowledge necessary to do their jobs safely, to assist mentors with the orientation process, and to develop a relationship with the department educator. The classes also connect new staff with other research colleagues, such as staff in the grants, finance, and IRB areas, who can serve as resources when questions arise later.

The course includes definitions of terminology and acronyms that often are unfamiliar to those with no experience in research, and the curriculum is divided into learning modules that can be taught in a classroom over a period of six to eight weeks. The modules start with basic research practices and build on each other.

The research educator for Spectrum Health recruited members of the research staff to teach various sections of the class to add their expertise and experiences to the material. The classes are also interactive, allowing for questions and discussion. The classroom is an ideal setting in which to deal with specific situations and best practices encountered through daily work.

Sites have an ethical obligation to support clinical researchers and equally to protect human subjects in research; to this end, training and continued education are necessary to conduct high-quality research.

FIGURE 1. Movies Reflecting Clinical Research Principles

Movie	Year	Research Topic
Miss Evers' Boys[10]	1997	Human Subject Research Protection/Vulnerable Populations
Awakenings[11]	1990	Phase I Research/Consent Issues
Lorenzo's Oil[12]	1992	Research and Development/Barriers and Conflict of Interest

During the orientation period, new staff may have experiences that relate to the topics being studied, which in turn lead to valuable discussions and learning. Key components of the Research 100 course include an overview of the CRC and principal investigator (PI) roles, good clinical practice, protocols, and investigator brochures. We also review the informed consent process, study startup activities (including IRB submission), source documentation and management, monitoring visits, and research study subject management (see Table 1).

The research educator works to modify each Research 100 course for the audience. This may involve adding elements such as a speaker on a specific topic of interest or incorporating a movie that deals with a research topic (see Figure 1), followed by a relevant discussion. Pre- and post-course self-assessments aid in identifying areas where more education is needed. Providing this program ensures that staff receive consistent information in a learning environment.

Training Methods

Over the last decade, this education program has developed and evolved in recognition of the need for continual education of all members of the research teams. Changes were made along the way to keep pace with growing regulatory demands.

With the admonition from a recent article on research staff training that "[e]ach individual involved in conducting a trial shall be qualified by education, training, and experience to perform his/her tasks"[6] in mind, we identified that education does not come in one-size-fits-all packages. Along with the understanding that adults learn at different speeds and through different methods, we recognized that our staff were significantly diverse in terms of their ages and skill sets. We therefore augmented the program with various tactics that would reach all learners.

Our modifications started with the Research 100 course. Classes had always started at the time of hire, but waiting four to six weeks actually helped learners, because they could bring experiences observed in practice back to the classroom. This fostered additional group discussion and the ability to connect current learning experiences with the subject material.

A new staff member now begins his or her orientation by shadowing a mentor in day-to-day activities, thereby gaining experience with research processes. During this period, new staff complete other core training requirements, including certification to handle and ship dangerous goods, human subjects research protection, and all necessary hospital-specific computer programs.

The next change was to incorporate an online learning system featuring modules that were assigned to new staff for review prior to lectures. Historically, Research 100 was solely based on classroom lecture with supporting reading assignments, but adding the online modules aided learners with comprehension and retention.

We then built in additional group discussion time, the viewing of a thought-provoking movie followed by review and discussion, and a hands-on project that allowed staff to work their way through exploring a protocol, writing an IRB application, and drafting an informed consent form. Through this process we touched all the major learning types—visual, auditory, and kinesthetic.[7]

To facilitate continual learning opportunities for experienced research staff, we incorporated additional opportunities, such as a monthly lunch hour lecture series that brings staff together to focus on in-depth topics (e.g., recruitment practices, characteristics of high-performing research organizations, feasibility, and PI involvement). The research department also supports staff attendance at local research conferences or occasional regional or national conferences.

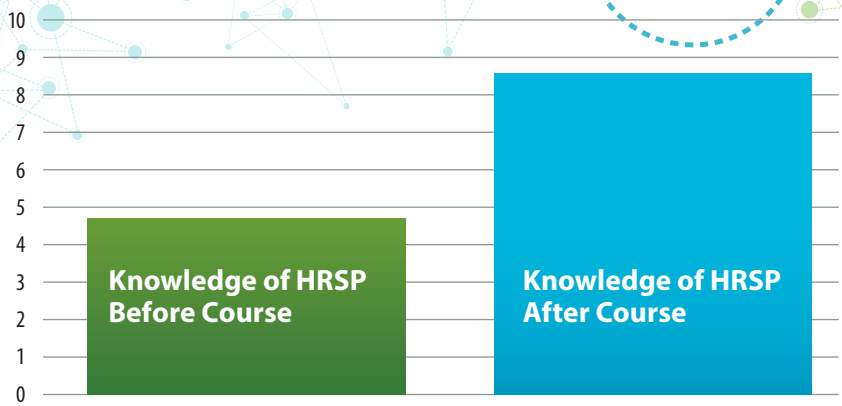
Forming a New Team

In the spring of 2013, a SWOT (strengths, weaknesses, opportunities, and threats) analysis was performed within the clinical research department. Weakness was defined as "items that hamper your work satisfaction and/or ability to perform your work." One of the identified weaknesses was a lack of adequate educational opportunities. We determined that new employees required a better education program, and that all staff should be mentored beyond the orientation period.

A part-time (20 hours per week), dedicated research educator position was implemented in response to this analysis, with the position being supported and funded by the central research department. Further, a Research Education Liaison

Because research staff typically were not hired with extensive research experience, the sites needed to provide the training and ongoing education to support the clinical trial activities.

FIGURE 2. Self-Assessment of Human Research Subject Protection Knowledge (n = 27)*



*0 = No previous knowledge, 10 = Extensive knowledge.

Team was created, with members including the new research educator and staff from a broad range of Spectrum Health departments.

The involvement of the team members in such extra-departmental work and their dedication to meeting on team business at least two hours per month is supported by management. Representation on the team of each clinical area provides staff with their own voice and brings forward their educational needs, ideas, and talents.

This team has been beneficial to the research department because it communicates to staff that we value their input, recognize their educational needs, and will respond accordingly.

Human Research Subject Protection Class

In an effort to encourage research knowledge within the institution, we also offer an education opportunity for those unfamiliar with research; individuals have the option to attend an instructor-led class designed to teach human research subject protection. An experienced clinical research nurse leads this class, which consists of online computer modules specific to research ethics.

Offered quarterly, this class has been ongoing for the last three years. The instructor teaches the content from the online computer modules, using specific examples of ongoing research studies within the institution, and then leads a group discussion following each module.

All staff members are invited to attend, as well as others outside the institution. This includes physicians, mid-level employees, registered nurses, and all other ancillary staff. Intended to promote a greater awareness of research within the organization, this initiative has created a culture of ethical research practices not only among research physicians and staff, but also among those providing direct patient care in the units.

Often this class stimulates questions from those interested in conducting research, as they are unfamiliar with the research process. We are able to offer guidance and education pertinent to the research process and navigation through the institution's research system.

We have also added a PI-specific education initiative that provides an overview of navigation of research at the institution. This 30-minute presentation added to the end of the Human Research Subject Protection class focuses strictly on the practicalities of doing research at our organization.

> Along with the understanding that adults learn at different speeds and through different methods, we recognized that our staff were significantly diverse in terms of their ages and skill sets.

By adding it to the end of this class, we are able to target new research personnel.

Attendees are now offered anonymous surveys at the completion of the Human Research Subject Protection class as part of an effort to identify areas of strength and weakness in the course. Many come to the course with little to no knowledge of the research process and, per survey results, complete the course feeling well-versed in the topic of ethics and research (see Figure 2).

Research Education Conference

Since 2007, we have offered four research education conferences that were open not only to hospital staff, but also to the community and other regional research professionals interested in or involved in clinical research. Such conferences usually begin in a large group setting and then proceed into smaller breakout sessions. The breakout sessions cover a myriad of topics meant for all levels of research experience, including research protocols, recruitment and retention strategies, IRB compliance, statistical design, grant proposal development, research ethics, and more. We have also had the privilege of having former research patients speak about their experiences in clinical trials. Physician and nursing continuing education credits are offered as part of the research education conference, as well.

These conferences offer professional development and education for our research staff, while increasing awareness of our research department and promoting a research resource within the community. The research conferences also allow for both internal and external networking for research professionals in the region, and have been well received by the research community.

To facilitate continual learning opportunities for experienced research staff, we incorporated additional opportunities, such as a monthly lunch hour lecture series that brings staff together to focus on in-depth topics.

Future Initiatives

Our plan for the future is to offer a monthly Journal Club to continue the learning experience by focusing on new trends and hot topics. In alternating months, the club will either meet in a live event or be held in an online format to allow for greater flexibility and attendance.

In addition, we plan to offer Research 200 classes to provide ongoing education to the research staff. These classes will examine advanced topics such as audits and inspections, statistics, locally conducted Investigational New Drug and Investigational Device Exemption studies, multicenter trials, and continuous quality improvement.

Recognizing the busy schedules of research department staff, we have considered offering these classes in a lunchtime lecture series format on consecutive days to allow for greater flexibility. We will occasionally offer contact hours to help facilitate nursing license and certification renewal.

We value, encourage, and support staff to become certified. Certification of CRCs and PIs by the Academy of Clinical Research Professionals, an affiliate of ACRP, denotes formal recognition of clinical research professionals who have met eligibility requirements and demonstrated proficiency of specific knowledge and job-related skills by passing a standardized exam. Evidence in the literature shows certification is valued by staff and employers, and may contribute to improved quality of patient care and enhanced collaboration among clinical teams.[8]

Within medical research, certification has been shown to potentiate protocol adherence and the quality of clinical trial work.[9] Research certification is supported by our institution as part of the overall tuition and certification benefit for all eligible employees. Research staff are reimbursed for fees associated with passing the initial exam and maintaining their certification every two years.

In the last five years, the number of staff achieving certification has increased from just three in 2008 to eleven in 2013. This trend is reflective of our commitment to education and the established program for staff, which emphasizes the importance of best practices and certification.

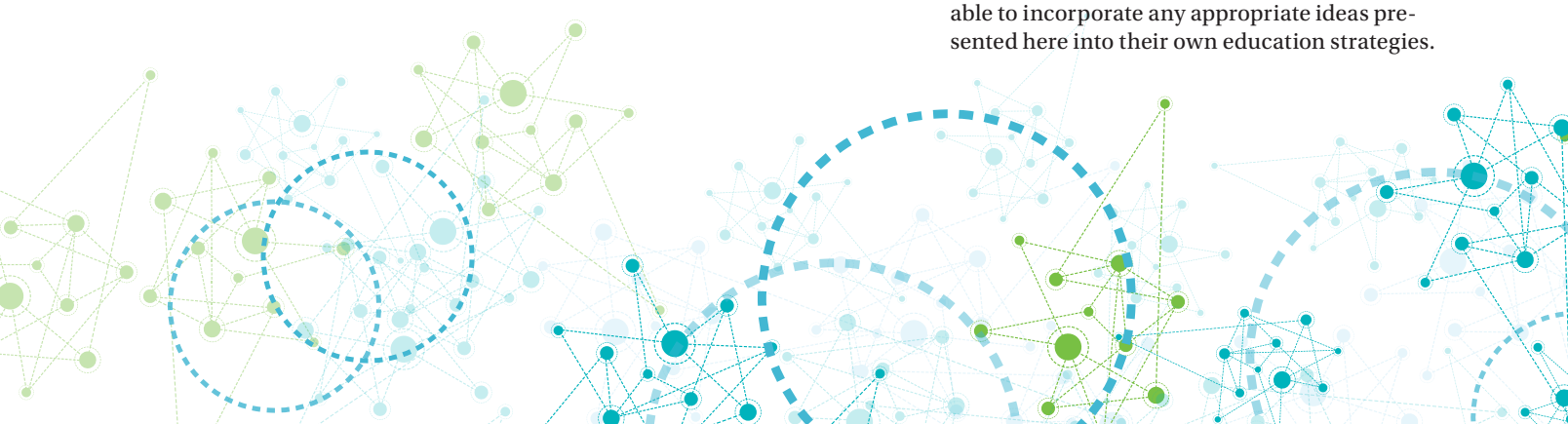
As part of the continuing growth of the research education program, we have offered our Research 100 classes to health professionals external to the research department who will conduct human subjects research. Encouraging outside departments to use our program helps everyone to standardize information, consolidate resources, and manage budgets responsibly. We hope in the future to offer the Journal Club and Research 200 to these external staff, as well.

Conclusion

Collaborative training and continuing education are necessary to conduct high-quality research, and personal and professional development of our staff remains a priority. Research staff education and training continue to be important parts of not only our initial orientation process for new research staff, but also as an ongoing effort to continue to develop and grow our experienced staff.

We will continue to develop and expand our Research 200 level classes and Journal Club, and to provide more educational opportunities to our larger research community. As research educators, we recognize our responsibility and obligation to educate our research community to promote clinical excellence and protect human subjects in research. In the future, we also plan to implement more measurable outcomes as a means of evaluating our research education initiatives over time.

We have found the techniques discussed here to be effective and beneficial in the education of research staff, and evidence in the literature supports the constructs of this program. Since education is such a key component of conducting high-quality research, we are sharing what we have learned in hopes that other institutions may be able to incorporate any appropriate ideas presented here into their own education strategies.



In an effort to encourage research knowledge within the institution, we also offer an education opportunity for those unfamiliar with research; individuals have the option to attend an instructor-led class designed to teach human research subject protection.

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Geeta Pamidimukkala, MS

Understanding the 510(k) Refuse to Accept Policy

The U.S. Food and Drug Administration (FDA) began implementing the new Refuse to Accept (RTA) Policy for Premarket Notification (510(k)) on January 1, 2013. This policy, which is outlined in the guidance document titled "Refuse to Accept Policy for 510(k)s,"[1] is intended to ensure 510(k) submissions meet a baseline level of completeness before the substantive review of the submission can begin.

Focusing FDA's review resources on complete submissions will provide a more efficient approach to ensuring that safe and effective medical devices reach patients as quickly as possible.

Focusing FDA's review resources on complete submissions will provide a more efficient approach to ensuring that safe and effective medical devices reach patients as quickly as possible. With the enactment of the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) and the Medical Device User Fee Amendments of 2012 (MDUFA III),[2] the FDA agreed to performance goals tied to the timeliness of reviews. Acceptance review, therefore, takes on additional importance in both encouraging quality submissions from submitters of 510(k) submissions and allowing FDA to appropriately concentrate resources on complete submissions.

Background

Prior to the enactment of MDUFA III, an analysis of the 510(k) review process revealed that the time it took FDA to reach a final decision remained consistent; however, there was an increase in the average number of review cycles and the total time to final decision (i.e., time shared between FDA and industry). This raised concerns that there were delays in the FDA's review of 510(k) submissions and led to an analysis of the first request for additional information, or AI request.

The AI request analysis revealed that approximately 80% of the first-round AI letters contained at least one deficiency related to the quality of the submission.[3] Examples of such deficiencies include clarification requests due to inconsistencies within the submission, or requests for basic elements that were missing in the submission. These submissions typically resulted in multiple rounds of review, which in turn resulted in an inefficient use of reviewer resources as extensive time was spent writing deficiencies.

As a result, FDA developed the new RTA policy. The policy aims to clarify the content needed in traditional, special, and abbreviated 510(k) submissions to allow FDA to conduct a substantive review, thereby enhancing the quality of received 510(k) submissions and improving overall review time. The content needed in each 510(k) submission type is provided in the form of criteria, listed in checklist format, for the traditional, special, and abbreviated 510(k) submission types. These checklists are included as an appendix in the RTA guidance document.

The basis for the criteria comes from existing regulations, cross-cutting and device-specific guidance documents, and standard review practices. The checklists are applicable to all device types that require 510(k) clearance prior to marketing.

Policy and Procedures

The information provided below is a brief summary of the policy and procedures described within the 510(k) RTA guidance document. Please refer to the guidance document for a complete discussion of the policy and procedures.

FDA staff will strive to conduct an acceptance review of all original 510(k) submissions and responses to RTA communications, but not on supplements or amendments submitted in response to AI requests. The FDA review clock and acceptance review begins only after the provided electronic copy (eCopy) is validated[4] and the appropriate user fee[5] has been paid. The assigned lead reviewer will select the applicable checklist based on submission type (i.e., traditional, special, or abbreviated), and will conduct the RTA review and make the RTA review decision within 15 calendar days of submission receipt.

If you have a question or an issue you would like addressed in a future column, please send it to Lee Truax-Bellows at ltb@ncra.com.

In order for the submission to be accepted, all criteria identified in the checklist must be present or a rationale should be provided for those elements determined by the submitter to be not applicable. As discussed in the RTA guidance document, the RTA review is an entirely objective review, and review staff have been trained to accept submissions that address each criterion, either by providing the requested information or including a rationale for an alternative approach.

Omission of information without a rationale is not interpreted as an implied determination that the criterion was deemed not applicable by the 510(k) submitter. Therefore, it is imperative that all criteria are addressed in order for the submission to be accepted. This policy ensures consistency and transparency of the RTA review across all device types. The adequacy of the provided information is assessed only after a submission is accepted for review (i.e., during the substantive review).

Once the acceptance review is complete and the decision receives supervisory concurrence, an automated e-mail is sent to the contact person listed in the submission. The e-mail serves as notification of the acceptance review decision and identifies the lead reviewer assigned to the submission.

If the submission is not accepted for review, a completed checklist is attached that indicates the information that was identified as missing in the submission. In the rare case that the RTA review is not completed within 15 calendar days of submission receipt, an automated e-mail is sent on day 16 to indicate that the acceptance review was not performed within 15 days, and therefore that the submission was deemed accepted. At that point, the submission moves to substantive review.

If the file is not accepted, the FDA review clock stops. The 510(k) submitter should respond to the not-accepted notification by providing the missing information identified in the checklist. The submitter should submit this information to be included in the submission under the originally assigned 510(k) number.

A new submission and new user fee are not necessary, nor is it necessary to re-send the entire 510(k) submission, unless FDA notes otherwise. It is sufficient to submit and address only the information requested per the checklist. If a response to the RTA notification is not received within 180 calendar days of the date of RTA notification, FDA will consider the 510(k) to be withdrawn and the submission will be closed in the system.

Upon receipt of the newly submitted information, the FDA clock resets and FDA staff should conduct the acceptance review again following the same procedure within 15 calendar days of receipt of the new information. The subsequent acceptance review will assess whether the new information makes the submission complete according to the checklist criteria.

If the submission is still found to be incomplete, FDA staff should notify the contact person and provide the new checklist indicating the missing item(s). There is no limit to the number of times the RTA review may be conducted for a 510(k) submission.

Once the submission is accepted, the FDA review clock continues and the submission is said to be under substantive review. The reviewer will assess the adequacy of the submitted information in the substantive review and may work interactively with the submitter or issue an AI request to address any deficiencies identified in the substantive review.

RTA Policy Highlights and Tips

- It is recommended that the submitter complete the RTA review him- or herself, using the appropriate checklist, and include this checklist in the submission, indicating the page number where each respective criterion is addressed. FDA has found that this practice can facilitate the RTA review.
- The RTA review is not an interactive process. The submitter should not send unsolicited information to FDA while the file is under RTA review.
- The lead reviewer will conduct the RTA review using the eCopy of the submission. Therefore, it is imperative that the eCopy be legible and complete. Figures, illustrations, and pictures should be clear and viewable in the eCopy.
- If the submission is missing information and is determined to be an "RTA not accepted" decision, the RTA response:
  - » Should address all the missing information in one response; a piecemeal approach will result in an "RTA not accepted decision"
  - » Should be submitted to the Document Control Center address as noted in the RTA notification e-mail; not to the reviewer
  - » Should include an eCopy and paper copy of the response
  - » Should be received by the Document Control Center within 180 calendar days from the date of the last "RTA not accepted" e-mail
- The submitter should reach out to the lead reviewer if it is not clear how to respond to a given criterion.
- The submitter should reach out to the 510(k) staff[6] in the following circumstances:
  - » If the submission was not accepted and the comments in the checklist include an assessment of the adequacy of the submitted content
  - » If the submitter disagrees with the RTA not-accepted decision
  - » If the submitter does not receive an RTA notification e-mail within 16 calendar days following submission receipt

References

1. Guidance for Industry and FDA Staff. Refuse to Accept Policy for 510(k)s available at www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm315014.pdf.
2. Information regarding MDUFA III, including the performance goals and commitment letter, are available at www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MDUFAIII/default.htm.
3. Analysis of Premarket Review Times Under the 510(k) Program. Report available at www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHReports/UCM263386.pdf.
4. Guidance for Industry and FDA Staff. eCopy Program for Medical Device Submissions. Available at www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf.
5. Guidance for Industry and FDA Staff. User Fees and Refunds for Premarket Notification Submissions (510(k)s). Available at www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM345931.pdf.
6. The Office of Device Evaluation Directory. Available at www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHOffices/ucm127854.htm#ODE.

Geeta Pamidimukkala, MS, wrote the Refuse to Accept Policy for 510(k)s and works on the 510(k) Program Operations staff of the FDA's Center for Devices and Radiological Health in Silver Spring, Md. The 510(k) staff may be reached at (301) 796-5640.

AN INTERVIEW WITH Greg Koski, PhD, MD,

President and CEO of the Alliance for Clinical Research Excellence and Safety (ACRES)

PEER REVIEWED
Laurin Mancour, CCRA, CCRP
[DOI: 10.14524/CR-14-00006.1]

For this issue of *Clinical Researcher,* I interviewed the President and CEO of the Alliance for Clinical Research Excellence and Safety (ACRES), a nonprofit organization operating in the public interest, which has entered into a strategic alliance agreement with ACRP to focus on the education, training, and credentialing of global clinical research professionals.

This partnership enabled the two organizations to join forces to address such mutually desired outcomes in clinical research as well-educated citizens, secure and efficient processes, transparent communication of credentials and certifications, and stronger professional development standards for clinical research professionals. A long-desired step toward these goals is the unification of standards and credentials, which is already taking hold as a trend in many industries and professions similar to drug and device development. The ACRES/ACRP agreement promises to be a significant and essential step toward realizing improvements in clinical trials on a global scale.

Q: How did ACRES and ACRP come to be involved with each other?

A: ACRP and ACRES have a strategic alliance to work together to realize each other's missions and visions. That relationship, in no small part, comes from those of us in the ACRES Executive Office having long been involved in ACRP. For recent examples, our general counsel serves on the ACRP Board of Trustees (as I have in the past); one of our vice presidents has just been appointed to the ACRP-affiliated Academy of Physicians in Clinical Research (APCR) Board of Trustees; and our chief operating officer has just completed his final term on the ACRP Board's Nominating Committee. Others of us have served on ACRP's Editorial Advisory Board and other committees. In short, it has been a longstanding relationship.

Q: What does this strategic alliance involve?

A: In addition to being a general agreement to support each other's work, there are specific projects on which ACRP and ACRES will collaborate, for example, supporting certification of clinical research professionals globally and the related education and training that involves. Beyond projects, and at least equally important, are leveraging the relationships of the two allies.

Q: How do you see that being realized?

A: Between ACRP and ACRES, there is an extensive international network that can help to transform the conduct of clinical trials—their safety, ethics, and efficiency. The areas of interest of the two organizations are naturally conjoined, and it is in the interests of both to take advantage of this. Both organizations contend with the issues of safety, quality, and efficiency in a multitude of regulatory frameworks and jurisdictions and promote industry best practices. Similar collaborations in other industries dealing with these issues can be seen as examples of how this kind of agreement can enrich all stakeholders involved.

The advantage of ACRP working so closely with ACRES is our global approach to the issues facing our industry. ACRES has taken a step forward and applied a global integrated systems approach to our goals, which grants some powerful efficiencies for the benefit of both parties.

Importantly, too, both ACRP and ACRES have relationships with a number of organizations, including other nonprofits, to encourage change without duplication of effort. This is change at an institutional level, but in consideration of the global nature and progressive educational developments of the industry, it is an essential and necessary step toward a more unified approach. Considering the digital, global environment we find ourselves evolving toward, now is the time to revise our current processes to be more sustainable and effective. Also, given the amount of resources these kinds of change-efforts take, this kind of alliance between organizations is a practical way of getting things done—collaboration, not competition.

Q: Because this issue of *Clinical Researcher* focuses on achieving excellence through education and training in clinical research, what is ACRES doing in addition to promoting certification of clinical research professionals and the supporting education and training that involves?

A: We in ACRES think of education and training as part of an overall system of development, that is, development in the sense of sustainability of clinical research wherever in the world it is conducted. That demands practical, real-world tools for all the stakeholders involved in research, including, but not limited to, the core clinical research team and the site. For education and training, it also means access and media, like e-learning.

Q: So will ACRES be providing training for members?

A: ACRES does not intend to provide training under this agreement. Rather, ACRES aims to support and promote more accessible and high-quality training and development options by working with our allies. For ACRES-affiliated sites, this begins with enhancing awareness of what educational and professional development tools are available through a range of providers. Using our relationships with sites to promote professional development of individuals and teams is one of the unifying goals of this partnership; sometimes that can be as simple as calling a valuable resource to someone's attention.

For example, one of our allies, HealthCare-Point, makes its repository of education—and a tool for tracking personal experience and training—available as one of the services offered to affiliated sites at no cost through the ACRES Global Network. The repository and its range of training available are impressive, and obviously of value to more than sites. By sharing that information through ACRP through communication to individual members, a valuable educational and professional development tool becomes more widely accessible, which benefits both sites and individual professionals.

Another example of how we approach development in an integrated systems perspective is the way we seek to guide industry practice through the establishment and promotion of sound policy and sound implementation—what we call our Foundation Initiatives. One of the initiatives is dedicated to establishing and promoting a Safety Culture, from adverse events reporting through risk evaluation and mitigation. Mere adherence to procedure may be technically adequate, but in order to ensure the best possible and most ethical clinical research, you have to embrace a more comprehensive "safety first" operating philosophy than we have now.

Building a Safety Culture requires a different mindset and operating behavior that takes human factors into account and covers a lot of ground that isn't necessarily addressed in regulation. It also includes translating methods and techniques from other industries, like aerospace and nuclear energy, where safety is paramount and "engineered-in"—safety by design.

Ensuring research subject safety is an absolute priority for everyone involved, but Safety Culture

ACRP and ACRES have a strategic alliance to work together to realize each other's missions and visions.

Using our relationships with sites to promote professional development of individuals and teams is one of the unifying goals of this partnership.

This is change at an institutional level, but in consideration of the global nature and progressive educational developments of the industry, it is an essential and necessary step toward a more unified approach.

has to be nurtured through promoting and championing specific practices. This means both structural change and learning how to implement it.

Two final thoughts on education and training:

- First, it's pretty obvious in our industry that education and training are clearly not limited to just classroom or remote kinds of learning. On-the-job experience and mentoring are critical to the success of both individuals and organizations. Understanding how professionals and organizations actually develop and sustain themselves—and using that knowledge to provide more effective programs—is essential to make the most out of scarce education and training resources.
- Second, members of the public—and the media that they rely on—need to better understand clinical research. ACRES recognizes that public education, as well as professional education, is an essential part of an integrated systems view of development and sustainability for our industry. Our Foundation Initiatives and other efforts always have public education in mind.

Q: You discussed the ACRES Foundation Initiatives. How will they help change how we do clinical research?

A: Simply put, these initiatives are the ACRES engine, as it were, to implement change to push quality in clinical research across the board. By identifying sound policy and best practices, we promote a higher quality product overall. In addition, by taking an integrated systems approach, they are intended to work together—in matrix fashion—so that the changes that are implemented are not piecemeal or counter to other promoted policies and practices.

We felt it was essential that these initiatives not be perceived as "silo" or piecemeal solutions, but as a comprehensive and well-integrated system of policies, standards, and practices with tools to support them effectively.

[Note: Articles in The Monitor *have addressed the concerns of organizational silos in clinical research, typically meaning the separation of functions in an organization into distinct and often-conflicting interests and purposes. Here, ACRES is also referring to silos between stakeholders in research, ranging from sponsors to research overseers, such as ethics committees and regulators.]*

Q: Do you mind going into more detail about the key operational initiatives that ACRES is developing?

A: The ACRES initiatives focus on sustainable best practices and implementation to achieve high-quality clinical research for the range of stakeholders that make up the research community. For example, the SASI (Site Accreditation and Standards Initiative) Steering Committee, which includes representatives from multiple stakeholders on a global level, has focused on basic performance standards in five key areas: personnel, information technology, ethics and integrity, standards, and facilities. Others, such as accrual and retention, will also be included.

Soon, a report will be published describing the work that has gone into SASI, as a prelude to convening a Global Stakeholders Consultation and creating working groups to develop specific standards in each of those critical areas. These working groups must represent all stakeholders—especially sites, sponsors, and regulators.

Once the first versions of standards have been developed, the Steering Committee will engage a much larger group of stakeholders to solicit feedback and hone the standards. The standards and practices will be "pressure-tested" in working environments before they are moved forward to a final set of accrediting standards.

We anticipate this process may take about three years, although we will already be nearly a year into it when this interview is published. We are also working in collaboration with other efforts, such as that of the Institute of Medicine, which is U.S.-focused, whereas ACRES is globally focused. However, in order for SASI to be a success, we have to establish accreditation as a valuable proposition.

Q: How is that process coming along?

A: In addition to promoting the value proposition and developing the standards, the first phase of affiliation with sites is also under way. ACRES has provided this affiliation free of charge, in order to remove any potential barriers to affiliation and eventual accreditation. To that end, last year we rolled out a new site network information interface, which allows sites to register as an affiliate of the ACRES network, indicating their commitment to excellence and safety and to move toward being qualified by adopting the quality, safety, and professionalism standards of SASI.

Any site interested in participating can visit a web-based platform and register for free to become affiliated. Doing so will include the site as a beta test site, granting it access to the system that allows

its staff to participate in training initiatives and contribute their perspectives to the network. Beyond affiliation and accreditation, this interface and system provide an efficient tool for sites to demonstrate their qualifications to sponsors, but there are other benefits, as well.

Q: What are some of the other benefits of sites registering their affiliation with ACRES?

A: Sites are provided with a set of tools for promoting compliance and improving productivity and sustainability. This includes applications that can allow sites to archive all of their experience and training records in a safe, secure, but sharable space. This information can then be shared with regulatory authorities, institutional review boards, and sponsors in a transparent yet secure environment.

With more than 148 clinical trial management system (CTMS) providers currently available, different formats may cause interoperability challenges for research sites. To promote consistent processes and information sharing, data need to be supplied, shared, and stored in a consistent manner.

Sites that register with ACRES will use safe, fully validated exchanges of electronic information, and will adopt Clinical Data Interchange Standards Consortium standards for their CTMSs. They will become beta affiliates that have opportunities to test some of the quality management applications and programs, including self-assessment tools, a standard operating procedure template library, and ultimately tools for accreditation support.

Eventual costs for supporting site accreditation must be low, since it will need to be an accessible value proposition for sites across a range of social, financial, and global environments. These processes and systems are intended to open doors and foster opportunity for all involved parties.

Q: How is ACRES focused on regulatory issues?

A: ACRES is also addressing regulations and guidance. Simplification and standardization have dominated the debate thus far, but regulatory innovation is no less critical to enable regulating authorities to keep pace with the speed of science and technology.

This is where the ACRES integrated systems perspective is invaluable. Our approach is to address simplification, standardization, and innovation simultaneously—another example of how thinking in terms of systems yields the most viable results.

Finally, any discussion of change in biomedical research and development regulation quickly finds itself immersed in risk-based and continuous quality concerns, which are addressed by another ACRES initiative.

Q: Since you personally have been so involved with ACRP over the years, is there anything else in particular our members might be interested to know about ACRES?

A: ACRES is not a trade association, professional society, lobbying group, or membership-driven organization. It is a nonprofit networked organization intended to promote and sustain superior quality clinical research while operating in the public interest.

On a practical level, ACRES seeks to engage all stakeholders in the extended clinical research enterprise in the public interest. In this sense, "public" means both the interests of our industry professionals and of the public in general, whose members depend upon our best efforts to improve their healthcare and quality of life.

The way we will accomplish our mission of change is systems-based, which in its most fundamental way means developing solutions to essential problems where the interests and processes of research constituents—stakeholders—are connected and interoperable. That way, unintended consequences don't create more problems than the solutions.

ACRES sees the research site as the fundamental building block of the system—like a personal computer connected to a larger enterprise network. Information is supplied, stored, archived, and used effectively to allow for the various requirements to be met (set by the various users and stakeholders in the system). However, in order for there to be appropriate standards and maximum efficiency, site-based systems need to be compatible with the other stakeholders in the network.

ACRES sees its efforts at unifying standards and promoting global site accreditation as fundamental to the network and constructive innovation. Furthermore, like ACRP and APCR, our mission is global, which means developing and redeveloping countries, as well—all nations that have clinical research as a public healthcare and economic priority.

ACRES aims to support unprecedented access to research to benefit every stakeholder. We look forward to a very productive, long-term relationship between ACRES and ACRP.

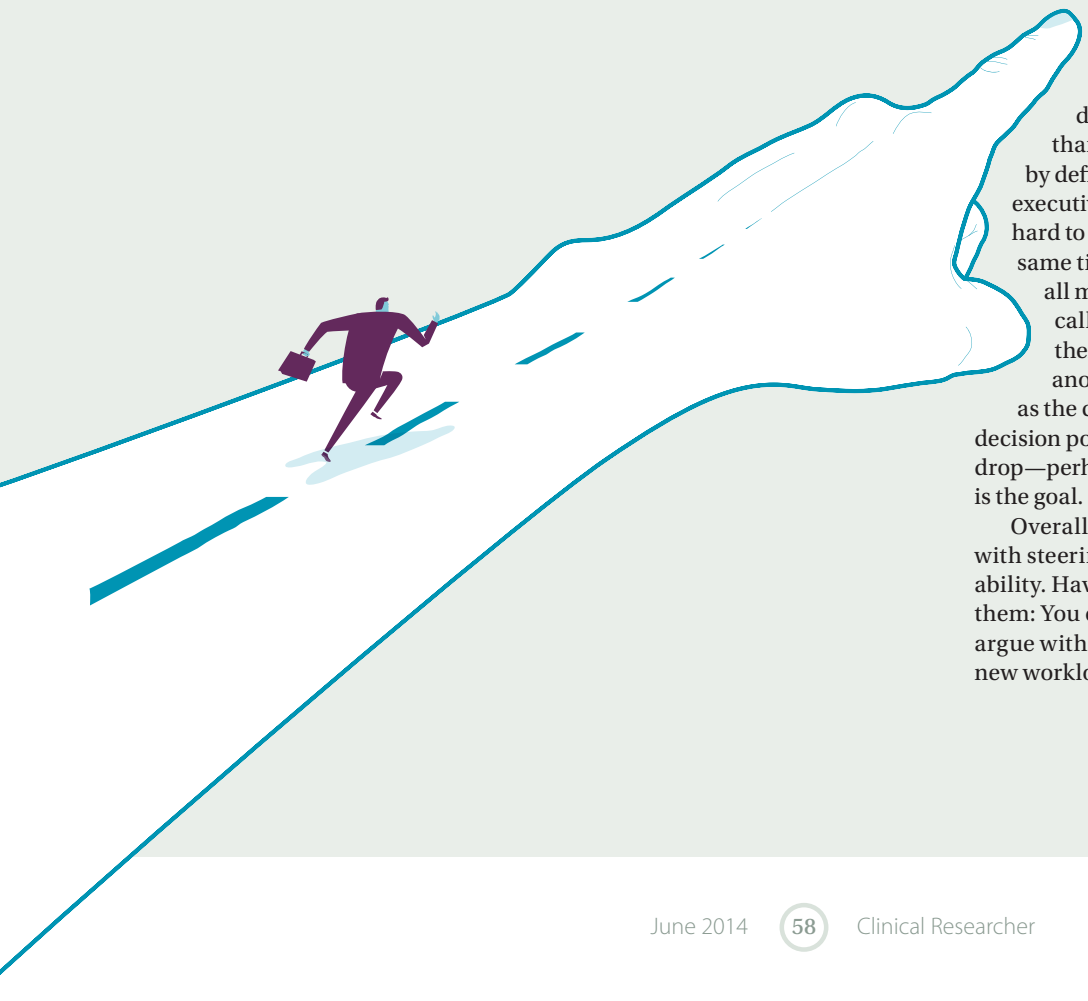
> The ACRES initiatives focus on sustainable best practices and implementation to achieve high-quality clinical research for the range of stakeholders that make up the research community

Laurin Mancour, CCRA, CCRP, is president and principal consultant for Atheneum Consulting, LLC, in Durham, N.C., and a current member of the ACRP Board of Trustees. In 2011 she also was the inaugural recipient of ACRP's Advancing Awareness in Clinical Research award. She can be reached at laurin.mancour@gmail.com.

Ronald S. Waife

Backseat Drivers

We commonly assume that the involvement of senior executives in a project will improve the performance of that project. To that end, we form "steering committees" of such executives to, presumably, steer the project to its shining destination. Too often, instead of steering, these committees are little more than backseat drivers: They can't see the road ahead, don't know the route, don't work the controls, and are lulled to sleep in the moving car. Like the classic backseat drivers, this position doesn't preclude them from shouting directions and complaining about the ride—even to the point of hoping that the car will just turn around and go back home.



Unintended Consequences

Steering committees are models of the "law of unintended consequences." Do we think we might co-opt our executives into supporting our project by forming an executive committee for them to sit on? Be careful what you wish for!

Depending on your company culture and individual executive personalities, your steering committee may turn into a new venue for interdepartmental conflict. It may draw unwanted, uninformed attention to a project the members did not know about and do not support. It might be the perfect forum for micromanagement. It is commonly the ideal mechanism for stalling, rather than enhancing, decision-making.

Even if you avoid these dire, unintended consequences, a steering committee is almost guaranteed to delay your timetable, if for no other reason than, since you created the committee, by definition it has to meet. Further, as an executive committee, by definition, it is very hard to get these folks in the same room at the same time on any regular interval. This leads to all middle managers' *bête noir*—executives calling in to committee meetings from their scratchy cellphones from their car or another continent, or both. As we know, as the committee meeting reaches a critical decision point, the cellphone call is guaranteed to drop—perhaps conveniently, if avoiding a decision is the goal.

Overall, the common experience of those living with steering committees is their pure unpredictability. Having formed them, you are stuck with them: You cannot ignore them, hurry them, or argue with them. By forming one, you've created a new workload for yourself with unclear benefit.

Steering committees are models of the "law of unintended consequences." The trick is how to anticipate whether and when you will need this important assistance.

The Value of a Steering Committee

A steering committee might be useful at three distinct points in a project:

1. In the very beginning, when money and staff resources, departmental alignment, the will to change, and priorities all need to be marshaled.
2. At the very end of the project, to dole out appropriate praise to those deserving staff, and to lead a serious lessons-learned effort that generates meaningful knowledge for the next project.
3. During a particularly dire crisis midstream, when only executives can decide about a change in direction, investment, cancellation, or expansion, often due to circumstances external to the project that the executives are in a unique position to know about and understand.

Each of these circumstances plays to the precise strength and purpose of executive guidance. Each can be critical to your project and the investments being made. The trick is how to anticipate whether and when you will need this important assistance.

These three circumstances are, at best, discrete moments. The beginning and end points of your project may be benign and easily handled. There may be no crises at all. In that case, if you are preparing for monthly steering committee meetings and living with the results, you are paying for insurance you may never need.

Other than these three points in time, what the steering committee most needs to do is to stay out of the way. One way toward that is to avoid scheduling regular steering committee meetings on some artificial, calendar-based schedule. Having regular, arbitrary meetings only invites and legitimizes the backseat-driving behavior. If a group meets regularly, eventually its members will feel obligated to do something, much like an auditor feels obligated to find something wrong. Nothing is more dangerous than a committee looking for a purpose.

An Alternative

Why are we worried about the impact of a steering committee on decision-making? This is both the heart of the frustration and the solution to the problem. We are mixing up "steering" and "deciding." You need not automatically abdicate authority to a steering committee because of its name or the rank of its members. It is precisely this abdication that makes this discussion so important.

Stalled or misguided decision-making undermines the hard work of clinical development professionals every day. You hurry to a deadline, only to find that people are not ready for the fruits of your labors. Only the most knowledgeable and best informed staff can make use of your work, and decide what and when to move forward.

In all but the handful of circumstances described above, why do you need a steering committee? Perhaps "steering committee" is the wrong term—you may not need to be "steered" at all, but rather advised, or helped.

Can a project or a trial use the advice of senior executives? Can you use their help in getting cooperation from their peers, additional funds, or scientific guidance? Absolutely; but clearly, that is not "steering." Indeed, perhaps we who are running the project should be in fact steering the steering committee—being alert to how they can help, and when.

We are the ones at the wheel, foot on the gas, eyes on the road. You may have even been down this road before, or one very similar to it. You have passengers who can help with the trip, and we welcome executives to come along for the ride. They will enjoy it and we will learn from them, but leave the driving to us.

Ronald S. Waife is president of Waife & Associates, Inc. (www.waife.com), and can be reached at ronwaife@waife.com.

You need not automatically abdicate authority to a steering committee because of its name or the rank of its members.

Pragmatic Research Design

PEER REVIEWED
Edwin Anderson, CCRP
[DOI: 10.14524/CR-13-00045R1.1]

Design is the most important aspect of any research study; no other factor can so clearly define or limit a scientific endeavor. Without careful consideration of the objectives and potential obstacles, the study can be flawed beyond repair, and its results are bound to be inaccurate or misleading. The quality of findings is directly determined by the quality of design, and any results are only as good as the question that inspired them.

As in any form of art, optimal study design is achieved by the selection of the proper tools and their implementation by a skilled team. If either of these elements is lacking, the research will suffer. The best staff available cannot save a poorly designed study, and no amount of resources can overcome a flawed design.

Our role as responsible researchers is to anticipate multiple obstacles of trial design in order to preserve the scientific integrity of the data and the safety of the patients involved. To make clinical trials more effective, we must reevaluate the purpose of our research, recognize current limitations, and use new techniques to produce efficient studies and useful results. Pragmatic trials offer us an additional set of tools and considerations to optimize study design.

A Complete Picture of Results

The most basic method of assessing the quality of any research project is an examination of its intended purpose and evaluation of how effectively it captures the appropriate endpoints. The goal of the endeavor should be the advancement of science by systematic acquisition of knowledge, a goal surpassed only by the safety of participants where human subjects are concerned.

It is the highest aim of clinical research to improve patients' lives and protect their rights while they participate in a study. Although most clinical research is concerned with identifying a cause or cure for a defined indication, the pragmatic researcher is also concerned with how the results could be used for maximum effect in real-world applications.

Clear identification of the outcome of interest is paramount in the selection of study design. To this end, studies may be distinguished by their goal and loosely defined as either a pragmatic or explanatory trial. Where the explanatory trial seeks to prove the efficacy of a treatment in the most rigorously controlled setting, the pragmatic trial is concerned with the effectiveness of this proven phenomenon in the less controlled clinical setting.[1]

The distinction between the two types of trials comes from the questions being asked: First, can it work, and second, will it work under less ideal, more realistic circumstances. To better understand the implications of this subtle shift, even the gold standard randomized controlled trial (RCT) must be viewed as limited when compared to the real world, and may benefit from pragmatic considerations.

Our role as responsible researchers is to anticipate multiple obstacles of trial design in order to preserve the scientific integrity of the data and the safety of the patients involved.

Limitation of RCTs

Many established benefits make RCT the most widely used design in clinical studies, but its main strength is the ability to control experimental variables. Because we do not have such control over real-world practice, this strength may limit the application of treatment. To this extent, control itself can be a limitation.

RCTs are by nature atypical, and their results may not be generalizable to the population. Although it is not the express intent of RCTs to emulate a true patient interaction, this aspect of the research may be overlooked in later discussion and policy making. It remains the responsibility of researchers to adequately employ the best study design, or at the very least to be aware of the limitations of the tools they are using.

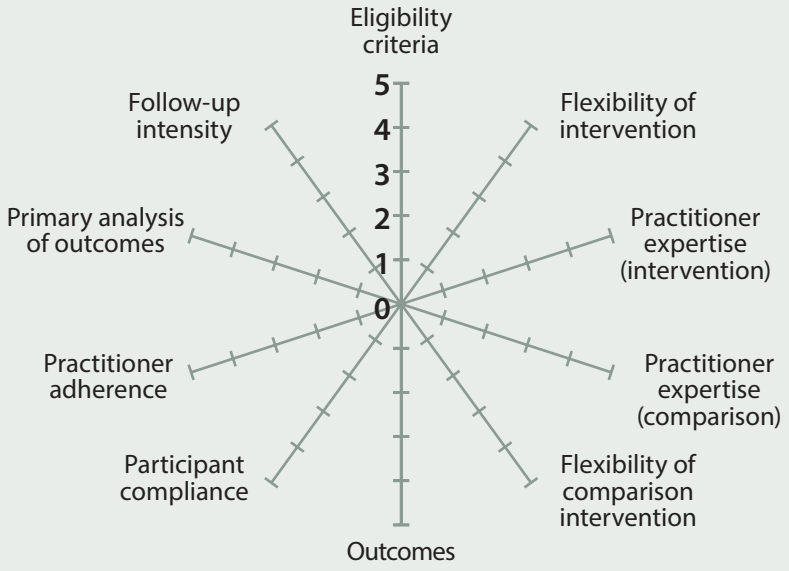
Consider the example of a typical industry-sponsored trial—a multicenter, placebo-controlled efficacy study with strict inclusion criteria. The sponsor likely provides materials, assessment devices, and specific drug preparation instructions for the trial, and, in many cases, these features are entirely reasonable. Predefined instructions protect the integrity of the study itself, while inclusion criteria are meant as safeguards to protect patients from health complications.

Even if such a trial is successful in arriving at positive outcomes, results are likely to be more internally valid than externally valid. This is because the nature of the experimental environment does not take into account the less ideal nature of real-world practice. For example:

FIGURE 1. A Comparison of Key Differences in Explanatory and Pragmatic Trial Types

Explanatory Trial	Pragmatic Trial
Determines efficacy of treatment	Determines effectiveness of treatment
Conducted in experimental setting	Conducted in realistic clinical practice
Highly selective, homogenous patients	Heterogeneous, typical clinic patients
PI trained for protocol, sees only study patients	PI skilled in practical patient care, ordinarily involved in care of participants
Short, complex follow-up	Long-term, standard-of-care follow-up
Often highly complex study design	Simple design, adaptive data capture
Requires strict adherence to treatment protocol	Physicians can more freely deviate, as is needed in normal practice

FIGURE 2. The Pragmascope*



**The Pragmascope was adapted from the PRECIS tool by Tosh et al. and provides a means to define studies based on a quantifiable scale of measure.*

Although most clinical research is concerned with identifying a cause or cure for a defined indication, the pragmatic researcher is also concerned with how the results could be used for maximum effect in real-world applications.

- Specialized devices may not be available in typical clinics, and the provided assessment scales may not reflect what is collected in routine practice.
- Strict exclusion criteria for an industry-sponsored RCT can unintentionally limit a population to the point where it is no longer representative of those who would actually be prescribed the investigational product in the future.
- Practices such as removing a patient for noncompliance protect data integrity, but neglect valuable information if that patient is not followed.
- Comparison to placebo in late-stage efficacy trials further reduces the data's usefulness, as opposed to a comparison to the drug's best competitor or in the setting of concomitant treatment.
- Industry protocols can include unrealistic timelines of assessments or encourage data-skewing competitive enrollment practices.

Pragmatic trials aim to counterbalance those areas that may undermine a study's results if left unchecked (see Figure 1). However, the majority of trials will not be entirely pragmatic or explanatory in nature. Neither is superior to the other; the distinction is made only to give the researcher finer control over what exactly is being investigated. It can be used as a tool to achieve the desired end. Realistically, all trials have features of both, but should maintain a balance between the two.

Pragmatic Tools of Measure

The distinction between effectiveness and explanatory trials was introduced in 1967 by Schwartz and Lellouch[2]; however, these terms have evolved over time. Recent developments in qualification and definition of these trial types began in 2006 with the Gartlehner Tool, a checklist with seven criteria for distinguishing efficacy from effectiveness studies.[3] The yes/no nature of the questions on this scale was imprecise, resulting in a general "good," "fair," or "poor" quality rating.

A further step was taken in 2008, with an extension of the CONSORT (Consolidated Standards of Reporting Trials) Statement, adding eight additional checklist items to the existing set of recommendations for reporting clinical trials.[4]

The PRECIS Tool (Pragmatic–Explanatory Continuum Indicator Summary), developed in 2009 for use during a trial's development stage, was the first practical means of incorporating pragmatic principles into the study design. By evaluating the degree of designated pragmatic or explanatory factors and plotting them on a 10-domain wheel, researchers were provided with a graphical representation of the nature of their study.[5]

Additional revision came in 2011, with the development of the Pragmascope tool (see Figure 2), which allowed researchers to better evaluate their study by quantifying the 10 aforementioned domains (now labeled from 0 to 5, rather than using a continuum). This improvement yielded not only a visual representation, but also a numerical score in which 0–15 equaled "explanatory," 16–35 equaled "balanced," and above 35 equaled "pragmatic."[6]

Using These Tools to Design Better Studies

Thus far, most articles about such tools have been retrospective, showing only how the tools can be used to evaluate current studies, instead of how to use them proactively to design balanced projects. Discerning the optimal study design at the outset of a project would greatly improve the quality of the endeavor, and trials that are more pragmatic in nature have the potential to be more directly relevant to the practices of clinicians.

To more naturally introduce these principles into study design, we might consider the conduct of academic research. Increasingly, there has been an effort to evaluate how clinics operate and how doctors perform in the clinic, as well as initiatives to increase communication across departments and eliminate unnecessary procedures. These same institutions have become advocates of quality control, cost reduction, and transparency with regard to patient treatment.

Using a design that incorporates aspects of how hospitals and clinics function could be more effective than providing atypical guidelines for physicians to follow for a singular research study. This is especially notable when a study's results are valid, but are otherwise unusable in that clinic's usual, day-to-day practice.

Allowing physicians to conduct their practice under less restrictive guidelines would result in more natural outcomes, and would provide valuable data points when a doctor deviates from a protocol—information that would otherwise be lost. Their setting, with all the variations in practice, is the most realistic measure of real-world effectiveness and a model to emulate when determining how a promising treatment can successfully be used in reality.

Although the strengths of pragmatic trials complement the weaknesses of RCTs, care should be taken to avoid the inherent limitations of an overly pragmatic trial. Selective application of these principles is key to answering the appropriate research question, as a poorly designed pragmatic trial is just as likely to yield misleading results. The primary limitations stem from their favoring clinical significance over statistical significance, and their practical implementation in less controlled settings.

Pragmatic trials also are a naturally weak tool for determining which aspect of a treatment plan is responsible for positive or negative results, and should not be used exclusively to determine the value of an intervention. Contrary to other study types concerned with public health outcomes, which rely on broad data collection, pragmatic trials pose the specific complication of attempting to capture intentional deviations in treatment application.

The inclusion of adaptive collection techniques could lead to data that are more difficult to report and analyze than in a comparable RCT with fixed data points. The reduction of enrollment criteria and extended follow-up practices would result in increased sample sizes, which may be difficult to manage longitudinally in both cost and effort.

Those interested in conducting research in a hospital setting should select a representative clinic—to avoid variation between programs—and should ensure that the practice possesses the appropriate resources to conduct the intervention. Study staff and project managers should have adequate familiarity with general research guidelines to avoid issues (such as bias) that are common to all studies.

All of these limitations should be recognized by designers and used as arguments in support of a balanced study design.

The application of pragmatic design elements may reduce the amount of overall research studies and shorten the time between a treatment's discovery and use in the clinic.

Summary

The success of a scientific breakthrough in the laboratory will always be governed by its clinical application, and even the most promising research can be crippled by an overlooked detail. More careful design would lead to more useful results, which could make a significant difference in a new finding's adoption as policy.

The application of pragmatic design elements may reduce the amount of overall research studies and shorten the time between a treatment's discovery and use in the clinic. Such a reduction could potentially reduce funding costs by limiting redundant research commissioned to investigate oversights of earlier studies.

In the case of a typical U.S. Food and Drug Administration application, it takes significant time and resources to develop a novel treatment. Even after years of investigation, only a predetermined standard of safety and efficacy information is known.[7] Every piece of new information, no matter how incremental, is valuable.

However, in a system of measured steps, the results must never be presented as overreaching what work was actually done. In an environment of limited resources for research, we must ensure each trial builds upon its predecessors toward the betterment of medicine, instead of unnecessarily replicating proof-of-concept studies.

Pragmatic principles should be applied appropriately, depending on the situation, and are not to replace current best practices for study implementation. Early phases should be conducted in routine fashion, but researchers should remain aware of their intentions as they progress into Phase III trials.

Evolving research questions should direct the design of pragmatic trial investigations, and tools (such as the Pragmascope) should be used as a means to that end. Although this process introduces a fundamental change in the objective of RCTs, it is not an additional step, and would be most efficient if incorporated into late-stage trials. In this way, the most meaningful studies are those that effectively bridge the gap between the classic RCT model and true clinical practice.

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FDA's (Lack of) Training Requirements for Clinical Trials

The best place to start when evaluating the training requirements for your organization is to review your site/corporate standard operating procedures and policies and determine what is required within your setting.

Q: What kind of training is "required" by the U.S. Food and Drug Administration (FDA) for staff involved in the conduct and management of clinical trials?

A: This is one of the most frequently discussed and misinterpreted questions that is asked regarding clinical trials. The Investigational New Drug regulations at 21 CFR 312.53 in the *Code of Federal Regulations* require that sponsors "…select investigators qualified by training and experience…." Similarly, the Investigational Device Exemption regulations at 21 CFR 812.43 require the "…selection of investigators qualified by training and experience…."

The FDA has never specified and described what this training should be, who should conduct the training, nor what topics should be covered or how often this training should be repeated. Certainly, the training should include the basics of good clinical practice (GCP), protocol-specific information, possibly disease-specific considerations, use of the investigational product (if applicable), and any other topics that assure that the study team has necessary training to be considered qualified to conduct the study.

The FDA offers neither certification in GCP nor guidelines on who should perform the training. FDA regulations regarding the conduct of clinical trials (21 CFR Parts 312 and 812 for pharmaceuticals and devices, respectively) are not that specific. The level of experience with both the type of product to be studied and the conduct of clinical trials can vary among studies.

The sponsor is also responsible for ensuring that all parties have all the information they require to conduct a specific clinical trial (312.55 and 812.45). Therefore, many study sponsors conduct their own training.

The investigator is also expected to ensure that any individual to whom a task is delegated is qualified by education, training, and experience (and state licensure where relevant) to perform the delegated task. The expectation is that investigators and sub-investigators will be knowledgeable about GCP, including human subject protection, data integrity, recordkeeping, etc.

The sponsor has discretion in determining what qualifications will be needed to conduct a study, and may identify in the protocol a required frequency of GCP training, in which case the investigator and sub-investigators would be expected to meet that frequency of training in order to comply with the sponsor's requirements.

FDA does have some information about available GCP training on its website. Both the Center for Drug Evaluation and Research and the Center for Devices and Radiological Health provide some limited online training relevant to clinical trials on their respective websites. Also, through its Critical Path initiative, the FDA now offers a Clinical Investigator Training Course targeted at medical professionals who participate in FDA-regulated clinical trials. This three-day course includes lectures given by senior FDA experts and guest lecturers from industry and academia; it provides FDA's perspectives on new safety concerns, adverse event monitoring, compliance with legal and ethical obligations of clinical research, and acceptable scientific and analytic standards in clinical study design and conduct.

The FDA also offers additional workshops and sessions on GCP and clinical trial expectations in cooperation with numerous professional organizations, such as ACRP, the Drug Information Association, Society of Clinical Research Associates, and others. Certainly, organizations such as ACRP offer a variety of training courses, programs, and certifications that provide training.

The best place to start when evaluating the training requirements for your organization is to review your site/corporate standard operating procedures and policies and determine what is required within your setting. If you feel that what is specified is overly burdensome or not meeting your needs, then modify your policies and move forward.

Do you have a GCP question or an issue that has come up at your site or company? If you are not sure of how to proceed, please send an email to: gcp@moriahconsultants.com and I will answer it in an upcoming column.

Q: What about requirements or suggested intervals for retraining during the course of a clinical trial?

A: Since there is no federal requirement for training for clinical research staff, there is also no requirement for staff (once trained) to be retrained at any particular interval, or even just once while a trial, no matter how lengthy, continues.

Certainly, many sponsor organizations and institutions require that a GCP update or retraining take place at certain intervals (typically every two years), in order to provide a refresher and update on changes that may have occurred to the regulations and industry practices. However, this is not an FDA requirement, and many people who are involved in the process will tell you that repeating the same basic introduction to GCP and documentation is probably not very useful or valuable.

Q: Other than sponsor-provided training, is it possible to obtain GCP and clinical trial training from other sources?

A: At the present time, there are a variety of sources of GCP and clinical trial training programs available. Many sponsors and contract research organizations have developed their own GCP training programs that they use for their projects.

Probably one of the biggest coordinated training initiatives is the Collaborative Institutional Training Initiative (CITI) at the University of Miami. This program was founded by two individuals from the university and the Fred Hutchinson Cancer Research Center in 2000, and has been expanded to include representatives from a number of other institutions with an initial focus on human subjects research in biomedicine. The program's biomedical human subjects research content was expanded in 2004 to include training and resources for social and behavioral researchers, including the addition of new institutions and experts.

Today, CITI is composed of an Executive Advisory Board and Program Advisory Committee and Developers Group to keep the content current. Institutions can purchase a subscription to the program and its different modules and use it for training their staff. The CITI training has hundreds of institutions as subscribers, is being used internationally, and is available on an individual subscription basis. More information can be found at www.citiprogram.org.

For training of individual investigators, coordinators, and monitors, ACRP offers its respected training courses and programs. In addition, it is possible to obtain certification from the Academy of Clinical Research Professionals, ACRP's affiliate body for certification, for individuals in these job functions upon passing a written certification examination. Check out the ACRP web page for more details.

There are also a number of vendors around the world offering various GCP and clinical research training course, either via online programs or at live seminars. There are so many programs available, it would be impossible to list them all here; just do a search on the Internet for GCP training.

Q: Is there any other type of training that is required at sites working on clinical trials?

A: Again, the FDA does not specify the training or even the types of training that may be needed for the proper conduct of a clinical trial. However, if your site will be involved in the shipment of biological samples and specimens, including routine blood and urine samples or tissue samples, you will likely need to use a commercial shipper, and there is a set of requirements for the proper packaging and label of all shipments containing biological specimens. Failure to properly package and label a shipment could result in the package not being accepted by the shipper.

The International Air Transport Association, an association of international airlines, has a set of guidelines and standards for the shipment of a variety of materials, including pharmaceuticals, perishables, and dangerous goods. The shipment of some of these materials requires knowledge on the specific requirements for the type of material. Usually, one can obtain all the information required for the proper shipment of your samples and specimens from the central laboratory involved in the study. Consult the study's laboratory manual for these details.

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The Challenging World of Research in a Digitized and Computerized Age

PEER REVIEWED | Yanwen Xia, PhD, CCRP

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The early 2014 deadline to attest to the meaningful use of electronic medical records (EMRs) has come and gone, so U.S. public and private healthcare providers and other eligible professionals are transforming paper medical records into EMRs to maintain their existing Medicaid and Medicare reimbursement levels. In the world of clinical research, paper case report forms (CRFs) have mostly become relics of the past, replaced by electronic versions (eCRFs) stored in systems such as Rave, InForm, and Oracle Clinical Remote Data Capture.

With the implementation of EMRs on the investigator side and eCRFs on the sponsor side, are we going to harness the full technological armamentarium in clinical trial data capture and verification? Will EMRs be up to the task of holding valid case histories of clinical research patients?

This article argues that there are still many daunting tasks on the investigator side before both sides can do away with paper, and discusses some of these challenges.

EMRs and Source Documents

According to the Food and Drug Administration (FDA),

> An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the [CRFs] and supporting data....[1]

All of these data elements can be found in an EMR system, but are still not adequate to construct the case histories for data verification.

The first challenge is: Are the medical records in the EMR system source documents? There are at least five basic methods by which records are populated in an EMR system:

1. Events are first recorded on paper and later transcribed into an EMR system.
2. Events are directly entered into the system, like the latest entry in an electronic patient diary (EPD) or an electronic signature entered by an investigator.
3. Automatic output from a system, like a lab report or a 12-lead electrocardiography printout.
4. Scanned-in or uploaded documents in PDF or GIF or Word format, such as pathology reports, X-ray reports, and CT scan reports.
5. Data transferred from one system to another, like transferring an EPD to an eCRF.

In an oncology clinic setting where multiple medical specialties are involved in patient care, source documents often originate from the office of a pathologist, a radiologist, a surgeon, a genetic counselor, or a patient's primary care physician. An oncologist receives them via fax or as an e-mail attachment or through other electronic media. Thus, from the way records are created in an EMR, not all data in an EMR system are source documents.

> Source documents are, according to the FDA, considered to be the original records or certified copies... [such as] original documents and records including, but not limited to, hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, X-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial.[2]

Regarding the relationship between source documents and electronic records, the FDA says, "when the original observations are entered directly into a computerized system, the electronic record is the source document."[2] This refers to the second method of populating an EMR.

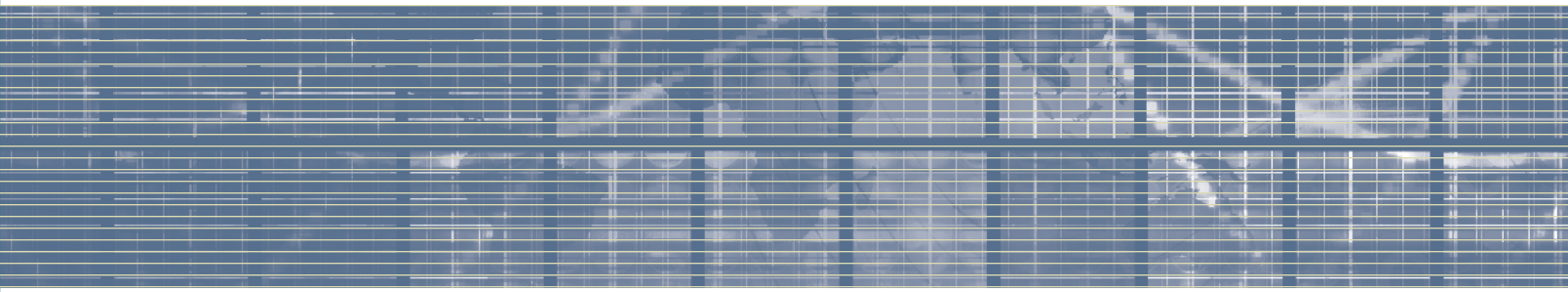
The FDA further clarifies that direct entry "means recording data where an electronic record is the original capture of the data. Examples are the keying by an individual of original observations into the system, or automatic recording by the system of the output of a balance that measures subject's body weight."[2]

According to definitions from the Guideline for Good Clinical Practice from the International Conference on Harmonization (ICH) for "source data" and "source document":

> 1.51 Source Data: All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).[3]

The ICH guidelines and the FDA all explain what source documents are and the different formats of source documents, but we expect further discussion on the special case of source documents in an EMR system. What should we do in regard to the real source if it is not stored in an EMR system? Many cases defy easy answers.

Very few EMR systems have the ability to record browsing history or electronic footprints showing which records have been viewed and which pages have been visited within the closed EMR system.



Seeking Clarity

A lot of data in the EMR are not first recordings. For example, in one EMR system, pathology and some other reports become part of the EMR system via the fourth method mentioned earlier, stored as scanned images.

If we define a source document as records on which clinical observations are first recorded, strictly speaking, many scanned and imported documents in the EMR system are copies of the first recording and should not be considered as source material. In fact, all scanned, copied, uploaded, imported, and transcribed documents are reproduced from the first recording, which usually exists in a paper format. These documents can be treated as sources only if the creator of the source confirms or certifies them.

The ICH guidelines and the FDA all explain what source documents are and the different formats of source documents, but we expect further discussion on the special case of source documents in an EMR system.

However, even if such documents are treated as sources, there is another potential problem: If a change is made to the original document, there is no automatic updating mechanism to keep the original and the scanned one synchronized.

Here are some examples of valid raw data as source documents in the EMR system. At my optometrist's office, there is a computer in each exam room. She enters her "original observations" directly into the system as she examines me. The test results from various modern gadgets also go directly into the system. I have also witnessed my primary care physician carrying a tablet instead of a paper chart. She wrote into the system as she was checking and chatting with me. A provider with either a laptop or tablet can capture medical data firsthand, "as it happens."

On the other hand, without a computer or laptop, providers have to jot down some notes while with the patient and later enter medical data into the system based on the notes they took. For example, a nurse will sometimes use a notepad or a piece of paper to record patients' vital signs and later transcribe them into the system. Strictly speaking, what this nurse enters is a transcription; still, we can consider what was later entered into the system as the source, because we have been treating this as source in all pre-EMR stages.

Questions Abound

What the nurse does regarding vital signs is in some way similar to what a physician does regarding progress notes. Very often, by the end of the day or during the day when the physician does not have patients, he or she dictates progress notes based on the personal notes previously written, his or her recollection of the visit, nursing notes, and lab reports.

However, not everything in the dictation is the source. The physician puts together information from various sources to compose the dictation. The sources include lab reports, nursing notes, CT scan report, and more. Both the nurse and the physician are creating documents at least partially based on first recorded notes on paper and reports of other sources. In both cases, the written notes are the source and what is later entered into the system is not exactly so.

Furthermore, if we accept the transcription of vitals as source documents, how about adverse events (AEs) and concomitant medication flow sheets, which the clinical research coordinator uses and updates while with the patient, and later updates the system with the new information? Because of this lack of clarification, we might have to rely on many note-to-files to define and confirm source documents in an EMR system.

The fact that not everything in an EMR system is source material poses a potential question for monitors visiting sites from sponsors or contract research organizations: When they do source data verification, do they stop at the system or go beyond it and trace back to the source? If they go back to the original documents, which part will they go to?

The mixing of source and nonsource documents in an EMR system also raises an issue for the site on retention of sources. Regarding record retention, the FDA says:

> An investigator shall retain records required to be maintained under this part for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.[4]

This issue cannot be clarified without first drawing a line between sources and nonsources in an EMR system and establishing a policy on retaining data in both paper format and computerized versions.

EMR System Must be Monitor-Ready

Another challenge is that an EMR system must be monitor-ready before it is used for data verification. Although it is easy to add to an existing system features to capture research-specific data like AEs, severe AEs, and concomitant medications, sometimes it is quite challenging to make an EMR system research- and monitor-ready. A system that is considered monitor-ready should at least be able to create a special user for monitors with:

- Read-only privileges and restricted maneuverability
- Restrictions on which patients' data an individual user can access
- Restrictions on viewing dates and times
- Disabling file downloading and file printing functions

Restriction on what users can view is the most difficult rule to enforce. The protection of patients' medical records works the same way as the protection of customers' data at any cloud storage company; when customers use cloud storage companies, employees at those companies can see all the data. Similarly, employees at healthcare institutions can access any patient's record within the institution; however, they are breaking the institution's rules if they are not authorized to do so. Even with these rules, no one can guarantee that rules will not be broken.

Within an EMR or eCRF system, when a record is created or changed, almost all systems have the ability to generate "time-stamped audit trails to independently record the date and time of operator entries and actions that create, modify, or delete electronic records."[5] However, very few EMR systems have the ability to record browsing history or electronic footprints showing which records have been viewed and which pages have been visited within the closed EMR system. Thus, very few systems can restrict which patients' data monitors can view.

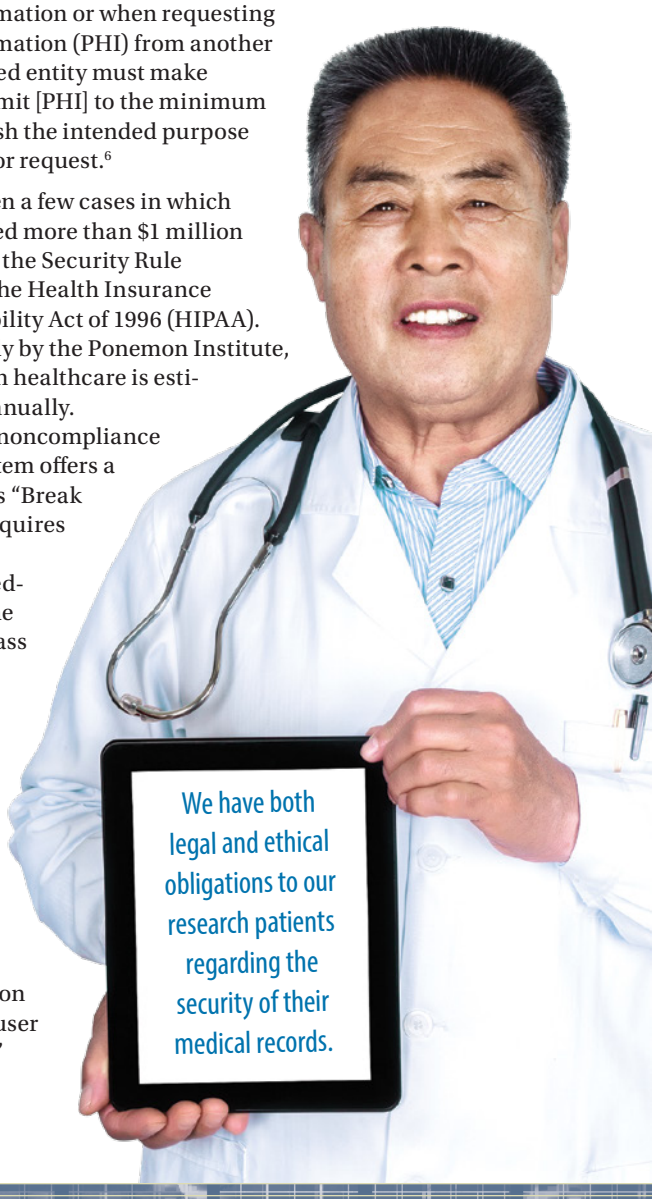
Who's Watching

It is one thing to trust that employees or monitors only view data for which they are authorized; it is quite another thing to run the risk of violating the *Code of Federal Regulations,* which includes a statement on "Limiting system access to authorized individuals":

> (a) Standard: A covered entity may not use or disclose protected health information, except as permitted or required by this subpart or by subpart C of part 160 of this subchapter.... (b) Standard: Minimum necessary—(1) Minimum necessary applies. When using or disclosing protected health information or when requesting protected health information (PHI) from another covered entity, a covered entity must make reasonable efforts to limit [PHI] to the minimum necessary to accomplish the intended purpose of the use, disclosure, or request.[6]

There have already been a few cases in which institutions have been fined more than $1 million for "potential violation" of the Security Rule defined and protected in the Health Insurance Portability and Accountability Act of 1996 (HIPAA). In fact, according to a study by the Ponemon Institute, the cost of data breaches in healthcare is estimated to be $6.5 billion annually.

In an attempt to catch noncompliance with HIPAA, one EMR system offers a functionality referred to as "Break the Glass (BTG)," which requires users to first declare their reasons for accessing a medical record. Specifically, the system sets up a virtual glass shield protecting patients' medical records. Any unauthorized attempt at accessing patients' records is seen as an attempt to break the shield. Once a reason is provided, an alarm is triggered so a security person can hear the sound of glass breaking, and an audit trail is in action following every click that user makes within the patients' records.



University of Kansas Hospital adopted this system to protect medical records of high-profile patients. Yale Medical Group uses it to catch any "unauthorized attempt to access an EMR" and alert Yale Information Technology Services. Texas Children's Hospital announced that it had begun BTG implementation in July 2013.

In an ideal world, all patients' medical records and all private data in a cloud storage company would be protected by a virtual shield. For some practices, it might incur some cost in performance and in system administration if the protection covers all patients.

It doesn't seem to be a huge challenge to implement the BTG functionality. We first define what "unauthorized" use is (e.g., a monitor accessing nonresearch patients is an unauthorized use), but the system will have to be more complicated than this when a monitor can access only certain types of research patients.

Protection of research patients' records entails more than that of regular patients' records. Access to the former records is granted not only based on the role of the user, but also on the study in which a patient is enrolled and is predefined. Also, the information technology (IT) team, in addition to grouping users based on their roles and responsibilities, must create a special user type for monitors.

Moreover, monitors are further classified according to the research trials they represent. Research patients are also categorized according to the studies in which they enroll. A restriction can be imposed based on the trial the monitor represents.

Making an EMR system research-ready is a challenge to the IT team, but it is definitely not impossible, especially with the BTG functionality. We have both legal and ethical obligations to our research patients regarding the security of their medical records. To fulfill these obligations, study sites should partner with their IT department to do whatever it takes to implement a proper audit trail for the viewing and modification of data, and to decrease the chances of unauthorized viewing of patients' medical records.

The challenges posed by EMRs do not end here. The onset of mobile technology makes it possible for both patients and care providers to remotely access medical records via a secure login.

Making Corrections on Uploaded Documents

A third challenge involves making corrections. Once again, the ICH states,

> 4.9.3 Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections (see 5.18.4 (n))... The investigator should retain records of the changes and corrections.[3]

The FDA also states "(a) Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records."[5]

It is easy to add a date and time stamp and to capture the username of the person who makes corrections to the eCRF to keep track of who, what, when, and why. In fact, electronic auditing features are advantageous over paper CRFs in tracking down data activities. It is also easy to create and modify data in conventional relational database systems.

However, when a PDF or a Word document is created outside the system and later is imported or uploaded into an EMR system, it is nearly impossible to make corrections to these read-only files. With paper medical records, physicians may make notes or corrections on their dictations. Many EMR systems do not support functionality by which the user can download and save the file to a local computer, make changes, and upload back into the system once the corrections have been made.

No End in Sight

From conversations with monitors, I have learned that currently most sites use EMRs; paper charts are on the way out. Sites grant monitors access to their EMR system, but even with EMRs, the sites still keep research folders holding study-specific documents like those devoted to AEs, serious AEs, concomitant medications, central lab reports, receipts for disk or lab submissions, tumor assessment worksheets, patients' informed consents, etc. The question is: Are they source documents? We used to store source documents with a patient's chart. After paper charts are replaced, where do we store them?

The challenges posed by EMRs do not end here. The onset of mobile technology makes it possible for both patients and care providers to remotely access medical records via a secure login.

When an EMR system moves beyond the realm of a company's Intranet and becomes a part of cyber reality, it will face further security risk and will require constant supervision from both security officers and the IT department. The potential risk is so great that U.S. Representative Patrick Meehan called in 2013 for the delay of launching EMRs into the wider cyber world, for fear of theft or abuse of Americans' personal information.

The true extent of the challenges ahead for research personnel is still unknown.

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Assurances and Certifications for Federally Funded Research

There are multiple assurances and certifications required when an investigator receives financial support for research from a United States federal department or agency. These assurances and certifications are described in detail by the U.S. Department of Health and Human Services (HHS) in its Public Health Service (PHS) Supplemental Grant Application Instructions,[1] and by the National Institutes of Health (NIH) in the NIH Grants Policy Statement.[2]

Federalwide Assurance

Each institution engaged in federally funded human subject research (with limited exceptions provided in the *Code of Federal Regulations* under 45 CFR 46.101(b)) must provide written assurance that it will comply with the HHS policy for the protection of human research subjects (45 CFR Part 46). In lieu of providing a written assurance for each application for federal funding, an institution can rely on an active Federalwide Assurance (FWA) on file with the Office for Human Research Projections (OHRP) within HHS.

Federally funded human subject research must be reviewed and approved by an institutional review board (IRB) registered with OHRP and designated as an IRB of record on the institution's FWA.[3] The IRB must consist of at least five members of varying backgrounds, including at least one member who is not affiliated with the institution.[4] Additionally, the IRB must follow written procedures:

> (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject… for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB and (ii) any suspension or termination of IRB approval.[5]

Further, NIH requires education in the protection of human research participants for all investigators receiving NIH funding for research involving human subjects.[6]

Research Misconduct

Each institution[7] that applies for or receives PHS[8] support[9] for research[10] must have policies and procedures in place that describe the institution's planned response to allegations of research misconduct.[11]

Research misconduct is defined as the "fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results."[12] As further defined:

- **Fabrication** is the "making up of data or results and recording or reporting them."[13]

Each institution engaged in federally funded human subject research (with limited exceptions) must provide written assurance that it will comply with the HHS policy for the protection of human research subjects.

- **Falsification** is the manipulation of "research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record."[14]
- **Plagiarism** is the "appropriation of another person's ideas, processes, results, or words without giving appropriate credit."[15]

There are two administrative steps an institution is required to follow whenever there is an allegation of research misconduct:

1. Called an "inquiry," the institution must sequester records, provide for procedural safeguards, and determine whether there is a "reasonable basis for concluding that the allegation falls within the definition of research misconduct."[16]
2. An institutional investigation must be completed within 120 days, ending with a final report submitted to the Office of Research Integrity.[17]

Conflict of Interest

Each institution that applies for or receives PHS funding must maintain an "up-to-date, written, enforced policy on financial conflicts of interest," and it must make this policy "available via a publicly accessible Web site."[18] The institution must require each investigator involved in PHS-funded research to complete conflict-of-interest training at least once every four years[19] in addition to disclosing all significant financial interests annually.[20]

Other Assurance and Certifications

In addition to the requirements for an FWA, a research misconduct policy and procedure, and a mechanism to solicit and track significant financial interests, multiple other assurances and certifications must be verified by the signatory official at an applicant organization seeking PHS funding.

Many of these assurances and certifications are "if applicable," meaning that they apply to those applications for federal funding involving a specific type of research. Among these are provisions for vulnerable populations (pregnant women, human fetuses, neonates, prisoners, children); data and safety monitoring (multicenter clinical trials that involve risk); research on human fetal or human embryonic stem cells; inclusion of women and minorities; reporting race and ethnicity; ClinicalTrials.gov policy; vertebrate animals; lobbying; gene research; smoke free workplace (see *Pub. L.* 103-227); prohibited research (for example: human embryo, controlled substances, distribution of sterile needles, abortions); select agent research; and grant activities that may affect the environment and historic properties.[1]

Some additional assurances and certifications cast a wider net, and may apply to some or all of the personnel receiving federal funds and in very limited situations to the entire workplace, such as debarment and suspension, drug-free workplace, nondelinquency on federal debt, and human resource assurances of compliance (civil rights, handicapped individuals, sex discrimination, age discrimination).

Researching Applicability

If your organization receives federal funding for research, some (but most likely not all) of the assurances and certifications described in the HHS PHS Supplemental Grant Application Instructions[1] or NIH Grants Policy Statement[2] may follow the money. Unless your organization is an academic institution, it is unlikely that you are engaged in federally funded research to the extent that all of the possible assurances and certifications apply to your organization.

However, ignorance of the law is seldom an acceptable defense to noncompliance. You should review the PHS[1] and NIH guidances[2] if you are unsure which assurances or certifications may require action by your institution. Then, the published regulations are the next source of clarity. At the beginning of most regulations is a section on "applicability," delineating to which activities the regulation applies. For example, the conflict-of-interest regulations at 42 CFR Subpart F are triggered when "applying for" PHS funding, and to each investigator "who is planning to participate" in federally funded research (42 CFR 50.602).

Conclusion

The big four requirements for institutions receiving federal funds for human subject research (for example, hospitals participating in cancer cooperative group research) are:

1. assurance that the institution will comply with the HHS policy for the protection of human research subjects and will have a registered IRB provide initial and continuing review;
2. assurance that investigators have been educated in the protection of human research participants;
3. policies and procedures to investigate research misconduct involving federally funded research; and
4. a publicly accessible conflict-of-interest policy that requires investigators to disclose significant financial interests.

Other assurances and certifications may apply, and PHS and NIH funding documents and the relevant regulations ought to be reviewed to determine whether these requirements follow other federal funds.

References

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2. National Institutes of Health. NIH Grants Policy Statement. Available at http://grants.nih.gov/grants/policy/nihgps_2013/nihgps_2013.pdf.
3. 45 CFR 46.503.
4. 45 CFR 46.107.
5. 45 CFR 46.103(b)(4). Cf. 21 CFR 56.108(a) (parallel regulation for FDA-regulated studies).
6. NIH Policy. Required Education in the Protection of Human Research Participants. Available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.
7. 42 CFR 93.213.
8. 42 CFR 93.220.
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11. 42 CFR 93.300.
12. 42 CFR 93.103.
13. 42 CFR 93.103(a).
14. 42 CFR 93.103(b).
15. 42 CFR 93.103(c).
16. 42 CFR 93.307(d).
17. 42 CFR 93.310-316.
18. 42 CFR 50.604(a).
19. 42 CFR 50.604(b).
20. 42 CFR 50.604(e)(1).

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