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

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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 medicines and devices[2].

Quite curiously, though, the criteria for individuals who conduct human clinical trials are only very genera, with scant detail in the regulatory authority definitions. Previous versions of the Declaration of Helsinki[3] and ICH E6 GCP Guidelines[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 or not he or she has had previous training or experience in clinical research. For physician investigators, clinical research coordinators (CRCs) and clinical research associates (CRAs), there are highly regarded certification programs, but there are no formal regulations that define the educational or experiential requirements, and personnel certification is not mandated.

Turning of the Tide

The tide is beginning to turn, however. The latest version of the Declaration of Helsinki, dated October 2013, states that "medical research must be conducted by individuals with appropriate training and qualifications in clinical research"[3]. India is moving towards mandating certification for clinical investigators, but it is uncertain what competencies such certification will require. 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 the research team[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 have published articles and white papers or presented content at professional meetings, which have brought this message to light[7-10].

As the concept of competency-based education and training has spread to the development industry, many groups have produced lists of knowledge, skills and attitudes to define 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 lists of core competencies for translational research scientists[11]

- The International Federation of Associations of Pharmaceutical Physicians and the Academy of Physicians in Clinical Research, which have developed lists 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, which has defined a career development pathway for CRCs, CRAs and investigators that incorporates competency statements[14]
- The Regulatory Affairs Professions 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, based on the belief that the most effective method to ensure quality clinical trial design, conduct and compliance is to ensure that those responsible for the various aspects of a clinical trial are, in fact, competent.

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

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 that 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 May 2013 at the MAGI conference, which included participants from an even broader representation of the clinical research community, and another in June 2013 at the DIA conference. The JTF then worked through the summer of 2013 and presented its final report in October 2013 at the MAGI conference. A list of the participating organizations is found in Table 1.

The JTF used a process designed to acknowledge and incorporate inputs from the many participating organizations. It required reviewing the many competency statements and identifying

Table 1. Participating Organizations

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

Competency Domains, the broad categories of knowledge, skills and attitudes that are necessary to function within the field of clinical research. It was determined that all of the competency statements could be aligned within the eight Competency Domains shown in Figure 1.

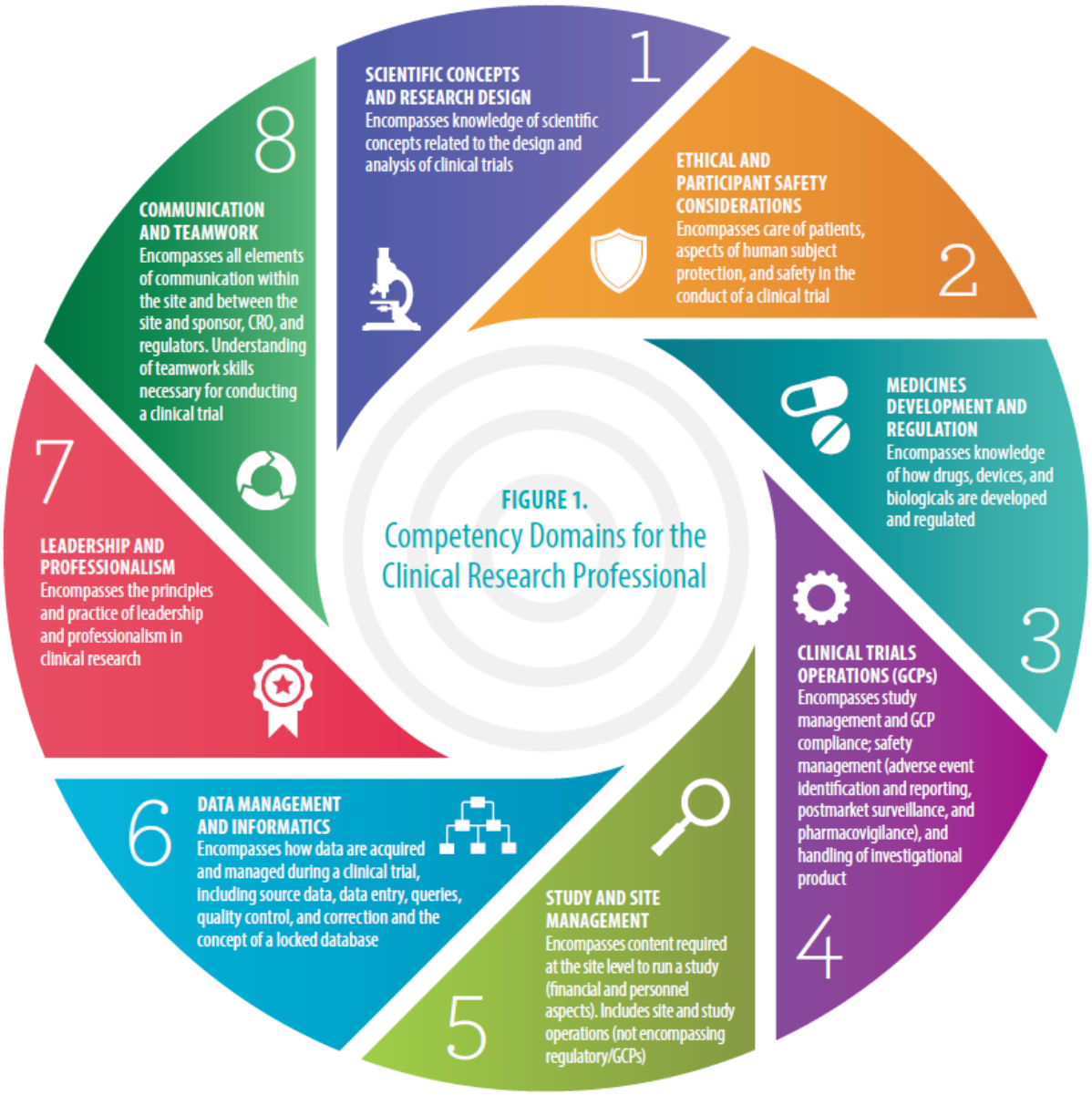

FIGURE 1.
Competency Domains for the Clinical Research Professional

The next step required assigning 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 the wording of the final KSA statements were inclusive and represented each individual organization's priorities, but were not redundant. The JTF decided that the harmonized competency statements at this level should reflect primarily the cognitive skills and that the performance or attitudinal aspects of learning objectives

were best defined at a more granular level by groups that would be using the harmonized competency statements as a framework to further develop focused expressions for specific purposes (e.g., job descriptions, accreditation criteria, training requirements). Collaborating organizations then had the opportunity to review the proposed competencies and domains. Comments and suggestions were integrated into a harmonized Core Competency Framework, which is presented in Table 2.

Table 2. Harmonized Core Competencies

Scientific Concepts and Research Design

- Demonstrate knowledge of pathophysiology, pharmacology and toxicology as they relate 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 they relate to the conduct of a clinical trial
- Compare the requirements for human subject protection 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 that ensure 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 variation and commercial aspects on 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 biologicals
- Describe the roles and responsibilities of the various institutions participating in the medicines development process
- Explain the medicines development process and the activities which integrate commercial realities into the life cycle management of medical products

- Summarize the legislative and regulatory framework that supports the development and registration of drugs, devices and biologicals and ensures their safety, efficacy and quality
- Describe the specific processes and phases that must be followed 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 (GCP's)

- 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 Good Clinical Practice Guidelines
- Evaluate the design conduct and documentation of clinical trials as required for compliance with Good Clinical Practice 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 product
- Differentiate the types of adverse events that occur during clinical trials, understand the identification process for AEs and describe the reporting requirements to IRB's/IEC's, 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 of monitoring for the study
- Describe the role 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 post-marketing 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 of study site organization to manage patient recruitment, complete procedures and track progress
- Identify the legal responsibilities, issues, liabilities and accountability that are involved in the conduct of a clinical trial
- Identify and explain the specific procedural, documentation and oversight requirements of principal investigators, sponsors, CRO's and regulatory authorities that relate 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 (EDC) 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 SOPs 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 impact 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 non-scientist community
- Describe methods necessary to work effectively with multidisciplinary and inter-professional research teams

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Implementation of the Harmonized Core Competency Framework

The Core Competency Framework can be used in many ways to improve the quality and safety of the clinical research enterprise; for example, to define criteria used by professional certification and site accreditation agencies. The Core Competency Framework can be used to formulate accreditation standards for academic programs to both standardize curricula and to ensure that programs are sufficiently comprehensive.

The greater challenge is to implement this conceptual framework in clinical research design and conduct. A comparison of two different types of studies reveals differences in competency requirements. For instance, when an investigator-initiated observational trial is compared to an industry-sponsored pre-market interventional clinical trial, it is possible to see how the Framework might be used to qualify a principal investigator. As illustrated in Table 3, the competencies for the Study and Site Management Domain are identical, but not so for the Scientific and Research Design Domain.

Table 3: Competencies and Study Methods

	Study Design	
	Observational	**Interventional**
SCIENTIFIC AND RESEARCH DESIGN DOMAIN		
Demonstrate knowledge of pathophysiology, pharmacology and toxicology as they relate to medicines discovery and development	Optional	Required
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 DOMAIN		
Describe the methods utilized 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
Apply management concepts and effective training methods to manage risk and improve quality in the conduct of a clinical research study	Required	Required
Utilize elements of project management related to study site organization 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 principal investigators, sponsors, CROs and regulatory authorities that relate to the conduct of a clinical trial	Optional	Required

This comparison does not imply that a less competent trialist can perform an observational study, only that certain competencies are not 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, then it is up to the principal investigator, study sponsor, and interested regulatory authority to ensure that the study team member possesses the necessary competencies to carry out his or her tasks. If additional knowledge or skills are identified, appropriate training can be obtained.

As a second example, Table 4 illustrates how one could utilize the Core Competency Framework to define the Good Clinical Practice knowledge requirements for an interventional clinical trial based on the functional roles of a principal investigator, CRC or CRA.

Table 4. Competencies by Principal Investigator, CRC and CRA Roles

CLINICAL TRIAL OPERATIONS DOMAIN			
	PI Role	**CRC Role**	**CRA Role**
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 bygood clinical practice guidelines	Required	Required	Required
Evaluate the design conduct and documentation of clinical trials as required for compliance with good clinical practice 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 product	Required	Required	Required
Differentiate the types of adverse events 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 role and process of monitoring for the study	Required	Optional	Required
Describe the roles and purpose of clinical trial audits	Required	Required	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 DOMAIN			
Describe the methods utilized to determine whether or	Optional	Optional	Optional

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	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
Utilize elements of project management related study site organization to manage patient recruitment, complete procedures and track progress	Required	Required	Optional
Identify the legal responsibilities, issues, liabilities and accountability that is involved in the conduct of a clinical trial	Required	Required	Required
Identify and explain the specific procedural, documentation and oversight requirements of principal investigators, sponsors, CRO's and regulatory authorities that relate to the conduct of a clinical trial	Required	Optional	Required

Table 5. Potential Utilizations and Outcomes

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

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. It is obvious that all members of the clinical research team do not require the highest level of competency in all of the areas listed, but these harmonized core competencies can provide a basis for developing more specific statements of knowledge, skills and attitudes required by clinical research professionals for more focused purposes. The categorization 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 better definition of career tracks and performance evaluations. Table 5 lists just some of the possible uses and outcomes that could result if the clinical research enterprise adopted and utilized the harmonized Core Competency Framework.

Once the Core Competency Framework is more broadly accepted, the JTF plans to approach the regulatory bodies of the world for recognition and acknowledgment of the Framework. Eventually, the document and its future evolutions could be housed by the International Conference on Harmonization as a guideline similar to the E6 Guideline for Good Clinical Practice[4].

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