Moving from Compliance to Competency:

A Harmonized Core Competency Framework for the Clinical Research Professional

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CenterWatch

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, there are only very general requirements and scant detail in the regulatory authority definitions of the criteria required of individuals who are responsible for the conduct of human clinical trials. 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/she has had previous training or experience in clinical research. For physician investigators, clinical research coordinators (CRCs) and clinical research associates (CRAs), there are certification programs which are highly regarded, but there are no formal regulations which define the educational or experiential requirements and personnel certification is not mandated. 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 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 which 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 medicines development industry, many groups have produced a listing of knowledge, skills and attitudes which 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 institutions in the U.S. which have developed listings of core competencies for translational research scientists,[11] the International Federation

FIGURE 1: Joint Task Force for Clinical Trial Competency Contributors and Collaborators

Joint Task Force for Clinical Trial Competency

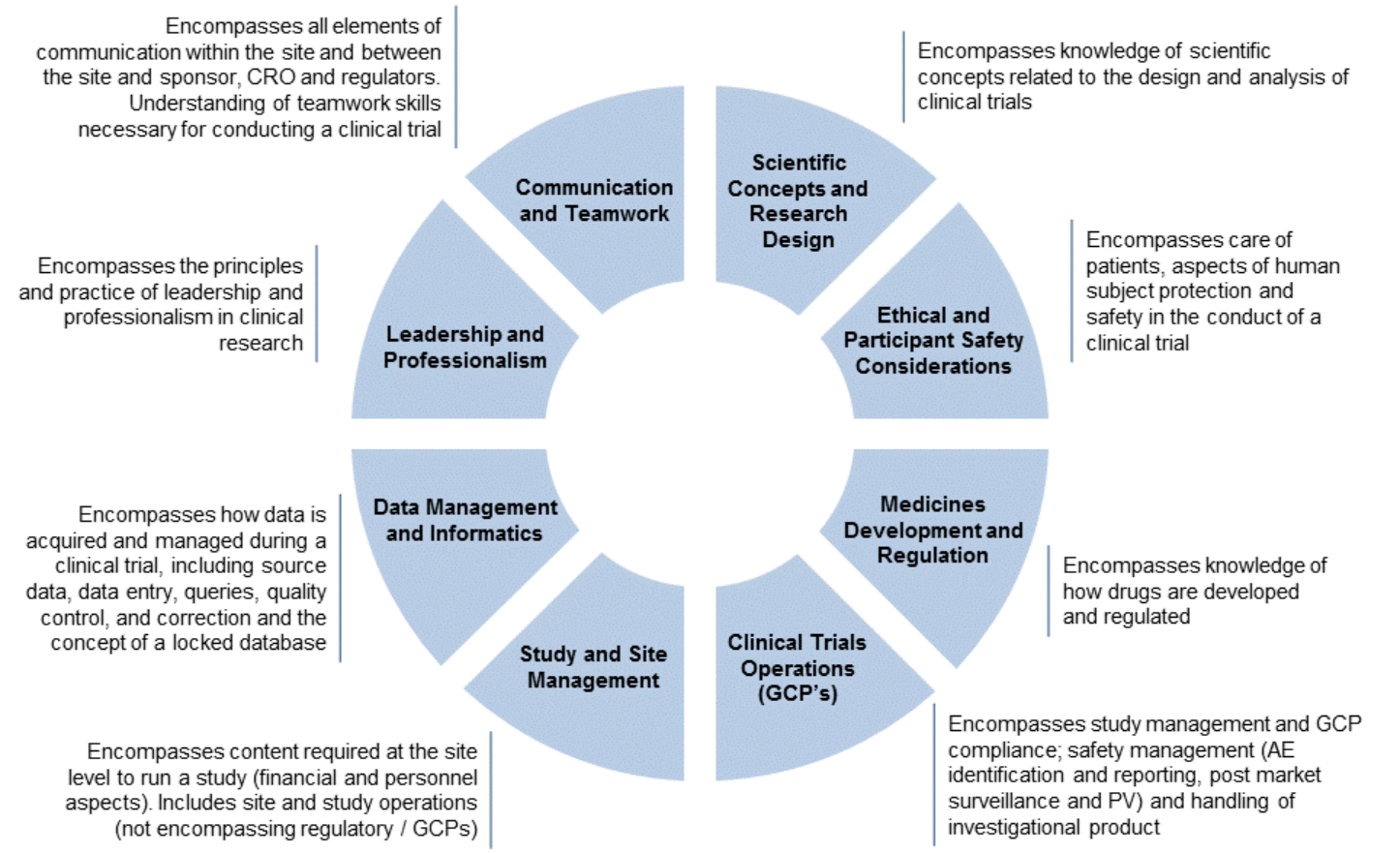
of Associations of Pharmaceutical Physicians and the Academy of Physicians in Clinical Research have developed listings of core competencies for pharmaceutical physicians and clinical investigators,[12,13] the Consortium of Academic Programs in Clinical Research has developed core competencies for graduates of academic programs and to guide curriculum development,[7] the Association of Clinical Research Professionals has defined a career development pathway for CRCs, CRAs and investigators which incorporates competency statements,[14] and the Regulatory Affairs Professionals Society has adopted core competency statements that relate to regulatory affairs professionals.[15] Furthermore, professional nursing in the US 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.

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 Trials Center at Harvard University during spring, 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 more 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 collaborating organizations is found in Figure 1. The JTF then worked through the summer of 2013 and presented its final report in October 2013.

The process used by the JTF was designed to acknowledge and incorporate the inputs from the many participating organizations. It required reviewing the many competency statements and identifying Competency Domains, or broad categories of knowledge, skills and attitudes which are necessary to function within the field of clinical research. It was determined that all of the competency statements could be aligned within eight Competency Domains which are listed in Figure 2.

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 or repetitive. It was decided that the harmonized com-

FIGURE 2: Competency Domains for the Clinical Research Professional



Joint Task Force for Clinical Trial Competency

TABLE 1: Harmonized Core Competencies for the Clinical Research Professional
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 hypothesis, 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 which 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
• 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 which 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 which supports the development and registration of medicines, devices and biologicals and ensures their safety, efficacy and quality
• Describe the specific processes and phases which 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 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 which occur during clinical trials, understand the identification process for AEs and describe the reporting requirements to 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 post-marketing phases of clinical research

petency 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 which would be using these harmonized competency statements as a framework to further develop the focused expressions for specific components of the enterprise (e.g. job descriptions, accreditation criteria, training requirements). The JTF and collaborating organizations were then given the opportunity to systematically review the proposed competencies and domains. Comments and suggestions were integrated into the final product which is presented in Table 1.

TABLE 1: Harmonized Core Competencies for the Clinical Research Professional (continued)

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 accountability that is involved in the conduct of a clinical trial
• Identify and explain the specific procedural, documentation and oversight requirements of principal investigators, sponsors, CROs and regulatory authorities which 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 which 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
• 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 which 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

Moving Toward the Future: Implementation of the Harmonized Core Competency Framework

The Core Competency Framework can be used in many ways toward improving the quality and safety of the clinical research enterprise; for example, to define certification criteria used by personnel or site certifying agencies. The Core Competency Framework could be used to formulate accreditation standards for academic programs to both 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. 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, when an investigator-initiated observational trial is compared to an industry sponsored pre-market interventional clinical trial; it is possible to illustrate how this framework might be used to qualify a principal investigator. As illustrated in Table 2, the competencies for the Study and Site Management Domain are identical, but not so for the Scientific and Research Design Domain.

This does not imply that a less competent trialist 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, 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 the selected protocol defined tasks. If additional knowledge or skills are needed, this would be the proper place to integrate with training programs

TABLE 2: Competencies and Study Methods		
Domain	**Study Method**	
	Observational	**Interventional**
Scientific and Research Design Competency		
• 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 hypothesis, 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 Competency		
• 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 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 is 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 which relate to the conduct of a clinical	Optional	Required

TABLE 3: Illustrating Clinical Trials Operations Domain Competencies by PI, CRC and CRA Roles			
Clinical Trial Operations Domain	**Principal Investigator**	**Clinical Research Coordinator (CRC)**	**Monitor (CRA)**
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 Good 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
Understand appropriate control, storage and dispensing of investigational product	Required	Required	Required
Differentiate the types of adverse events which 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
Understand the role and process for monitoring of the study	Required	Optional	Required
Understand the roles and purpose of clinical trial audits	Required	Optional	Required

TABLE 3: Illustrating Clinical Trials Operations Domain Competencies by PI, CRC and CRA Roles (continued)

Clinical Trial Operations Domain	Principal Investigator	Clinical Research Coordinator (CRC)	Monitor (CRA)
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
Describe the methods utilized 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
Utilize elements of project management related to organization of the study site to manage patient recruitment, complete procedures and track progress	Required	Required	Optional
Understand 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 which relate to the conduct of a clinical trial.	Required	Optional	Required

that have training materials and processes which are harmonized to the protocol-specific competency requirements.

As a second example, Table 3 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 a CRA.

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 which 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 competency in all of the areas listed, but these harmonized core competencies can provide a basis for development of more specific statements of knowledge, skills and attitudes required by clinical research professionals in more 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, better definition of career tracks and performance evaluations. Table 4 lists several of the possible uses and outcomes which can result from the adoption and utilization of the Harmonized Core Competency Framework by the clinical research enterprise and global regulatory authorities.

It is the desire of the JTF to approach the regulatory bodies of the world for recognition and acknowledgment of the Core Competency Framework and to ultimately house the document and its future evolutions within the International Conference on Harmonization as a guideline similar to the E6 Guideline for Good Clinical Practice.[4]

Acknowledgements

The authors would like to acknowledge Jason Nyrop (Deloitte, Inc.), for his expertise in production of the graphics and tables included; Norman Goldfarb (MAGI), Jim Thomasell (ACRP) and Jennifer Webb (DIA) for their support in facilitating the meetings of the JTF; and Jacquelyn Murphy of the Harvard University Multi-regional Clinical Trials Initiative for her administrative support.

TABLE 4: Potential Utilization and Outcomes of a Harmonized Core Competency Framework

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

References

1. Getz, KA. Assessing the downstream impact of protocol design complexity. *Touch Briefings.* 2009:93-95. www.touchbriefings.com/pdf/3322/kenneth-a-getz.pdf. Accessed March 5, 2011.
2. Getz KA. Drowning in sea of regulatory compliance. *Applied Clinical Trials.* 2007:16(2). http://appliedclinicaltrialsonline.findpharma.com/appliedclinicaltrials/article/articleDetail.jsp?id=401621. Accessed Feb. 1, 2007.
3. World Medical Association. Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. 2013. www.wma.net/en/30publications/10policies/b3/.
4. International Conference on Harmonization. ICH Tripartite Guideline: Guideline for Good Clinical Practice E6(R1). 1996. www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1_Guideine.pdf. Accessed Jan. 9, 2014.
5. Speicher, LA, Fromell G, Avery S, Brassil D, Carson L, Stevens E, Toms M. The critical need for academic health centers to assess the training, support and career development of clinical research coordinators: Recommendations from the clinical and translational science award research coordinator taskforce. *Clinical and Translational Science.* 2012; 5(6):470-475.
6. Carter, SC, Jones CT, Jester PM. Issues in clinical research manager education and training. *Research Practitioner.* 2007; 8:48-60.
7. Jones, CT, Browning, S, Gladson, B. Defining competencies in clinical research: Issues in clinical research education and training. *Research Practitioner.* 2012; 13(2):99-107.
8. Sonstein, SA. Core Competencies for entry-level positions in clinical research. 44th Annual Meeting of the Drug Information Association; June 22-26, 2008; Boston, MA.
9. Sonstein, SA, Silva H, Jones CT. Harmonization of core competencies across the clinical research enterprise to help enhance the quality of clinical trials and the personnel who conduct them. 48th Annual Meeting of the Drug Information Association; 2012; Philadelphia, PA.
10. Silva H. Challenges to clinical research in the USA and Latin America. 2009. Pan American Conference on Medical Education. Oct. 9-13, Buenos Aires.
11. Clinical and Translational Science Awards. Core competencies for clinical and translational research. 2011; www.ctsacentral.org/education_and_career_development/core_competencies-clinical-and-translational-research. Accessed March 22, 2013.
12. Silva H, Stonier P, Buhler F, Deslypere J-P, Criscuolo D, Nell G, Massud J, Kesselring G, van Olden R, and Dubois D. Core Competencies for pharmaceutical physicians and drug development scientists. Frontiers in Pharmacology. 2013; 4(105):1-7.
13. Koren M, Koski G, Reed DP, Rheistein PH, Silva H, Stonier P, and Seltzer J. APPI Physician Investigator Competencies Statement. *The Monitor.* 2011; 25(4):79-82.
14. Association of Clinical Research Professionals. Find Your Pathway. 2013; www.acrpet.org/MainMenueCategory/Education/Find-Your-Pathway.aspx. Accessed Dec. 30, 2013.
15. Regulatory Affairs Professionals Society. Regulatory Affairs Professional Development Framework: An Overview. White Paper. 2013. http://www.raps.org/portals/0/documents/pdf_framework_whitepaper.pdf.
16. Bevans M, Hastings C, Wehrlen L, Cusack G, Matlock, AM, Miller-Davis C, Tondreau L, Walsh D. and Wallen GR. Defining clinical research nurse practice: results of a role delineation study. *Clin Transl Sci.* 2011; 4(6):421-427.
17. Castro K, Bevans M, Miller-Davis C, Cusack G, Loscalzo F, Matlock A, and Hastings C. Validating the clinical research nursing domain of practice. Oncol Nus Forum. 2011; 33(2):E72-80.
18. Ehrenberger H, Lillington L. Development of a measure to delineate the clinical trials nursing role. Onc Nurs Forum. 2004; 31(3):E64-68.
19. Competency Framework Working Group. Competency Framework for clinical research nurses: A tool to promote patient safety and quality data. 2nd ed: Competency Framework Working Group; 2011: www.rcn.org.uk/_data/assets/pdf_file/0019/201466/Research_Nurse_Comptency_Framework-Version 2-Full-Oct_2011.pdf
20. Hastings C, Fisher CA, McCabe MA. The National Clinical Research Nursing Consortium. Clinical Research Nursing: A Critical resource in the national research enterprise. *Nurs Outlook.* 2012; 60(3):149-156.