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Overcoming inefficiencies in clinical research by fostering a systems approach and core competencies for biomedical professionals involved in medicines development

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SUMMARY

Clinical trials constitute the largest single component in medicines development, representing nearly 40 % of the related expenses. However, there is broad agreement that the current clinical trial system is inefficient. The biopharmaceutical industry, governments, regulatory agencies, academic researchers, the medical profession, and the media should work collaboratively and create efficient clinical trial networks. Clinical Research in Medicines Development (CR/MD) can be defined as an open system involving the above-mentioned stakeholders interconnected through a series of processes aimed to bring effective and safe medicines into the market. A systems approach is needed to overcome the current barriers to a cost/effective process including appropriate risk management. A simple conceptual model of an integrated system is proposed. The obstacles to implementation are also discussed.

Lack of an appropriately trained multi-professional workforce both in the industry-related and the academic clinical research field is also a significant part of the problem. The root of the problem resides in the lack of proper education in CR/MD at the undergraduate and postgraduate levels among academic institutions. Competency-based education has been proposed as a model for improving the quality and accountability for specific functions involved in the drug development process. Despite the growing awareness of competency-based education and the need for implementation of systems-thinking, its full adoption is still far on the horizon. Resistance to change is one of the obstacles to overcome. Continuing efforts to creating further awareness are key responsibilities of professional associations and academic institutions involved in CR/MD.

Key words: *Biopharmaceutical industry, clinical research, medicines development, competency-based education.*

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RESUMEN

Los estudios clínicos representan casi el 40 % de los gastos de desarrollo de nuevos medicamentos. Sin embargo, el sistema actual de investigación clínica es considerado ineficiente e insostenible. La industria farmacéutica, las agencias regulatorias, investigadores clínicos y académicos, la profesión médica y los medios de comunicación masiva deberían trabajar en colaboración para crear redes eficientes de sitios de investigación. La investigación clínica para desarrollar medicamentos (IC-DM) podría ser definida como un sistema abierto que incluye los elementos antes mencionados conectados a través de una serie de procesos orientados a traer novedosos

medicamentos efectivos y valiosos a la sociedad acompañados de un margen aceptable de seguridad y un buen manejo del riesgo. Proponemos un modelo conceptual de un sistema integrado pensante (SIP) así como los obstáculos para su implementación.
Por otro lado, la relativa falta de profesionales biomédicos adecuadamente entrenados en IC-DM tanto en la industria farmacéutica como en los centros de investigación clínica es parte del problema. La raíz de la situación reside en insuficiente educación y entrenamiento a nivel de pre y posgrado. La educación basada en competencias (EBC) ha sido propuesta como un modelo para mejor la calidad del desempeño y responsabilidad profesional en funciones específicas del proceso de IC-DM. Sin embargo, a pesar de la creciente aceptación de ambos conceptos (EBC y SIP) su adopción y/o adaptación están distantes, siendo la resistencia al cambio uno de los principales obstáculos. Las asociaciones profesionales e instituciones académicas deben contribuir con esfuerzos adicionales para crear conciencia de esta situación.

Palabras clave: *Industria biofarmacéutica, investigación clínica, desarrollo de medicamentos, educación basada en competencias.*

INTRODUCTION

The circumstances related to the COVID-19 pandemic underscores the role of the biopharmaceutical industry as a key link between basic biomedical discovery and the emergence of novel medicines that prolong or improve life. However, the industry faces several ongoing and emerging challenges, including technical knowledge gaps, limitations in clinical testing, lowered productivity, higher development costs, increased regulatory requirements, growing payer pressures, and patent expiration. Most large biopharmaceutical companies are compensating for this by shifting to alternatives such as merger and acquisition of other companies, outsourcing and fixed cost and personnel reductions, as well as broader collaboration with academia, contract research organizations, and nonprofit institutions (1-4).

An increased focus on growing new and emerging market revenue streams, including personalized medicine and rare diseases is also surging. Countries from the emerging world are increasingly involved in the global medicines development process and this is reflected in the growing number of publications and data supporting regulatory submissions worldwide. Local and regional enterprises are also blooming (4-6). Although the USA continues to lead new drug R&D globally, a regional focus on special therapeutic areas has emerged. China, India, and South Korea are emerging as important players in the global Research and Development (R&D) stage (7).

Clinical trials constitute the largest single component of the R&D budget of the biopharmaceutical industry, representing nearly 40 % of the R&D expenses of major companies. However, there is broad agreement that the current clinical trial system is inefficient.

Currently, each clinical trial is typically organized *de novo*, requiring substantial effort, cost, and time. Sponsors (Drug companies and Contract Research Organizations) must identify clinical investigators and assemble multi-investigational teams. Protocols must be written and submitted to each of many institutions, and approval of these protocols can take several months, without necessarily improving the scientific and ethical aspects of the study or the protection of study participants. Rising protocol complexity is hindering study performance, cost, and efficiency (8).

A wealth of published research details the inefficiency in the clinical research process. The Center for the Study of Drug Development at Tufts University documented the pitfalls in the overall process including significant delay in the site initiation process and incomplete accrual. Start-up times for trials varied widely, from 1.2 to 7 years, and the longer a trial took to begin, there was less likelihood that accrual numbers would be achieved (9,10). Examples of the dysfunctions and inefficiencies in the clinical trials system are given by the following figures commonly cited by clinical trial professionals:

- Less than 1 % of all medical doctors are ever involved in such trials.
- 40 % of active clinical investigators will only participate in one single industry-sponsored clinical trial in their working life.
- 30 % of all study sites involved in sponsored trials are not contributing a single patient.

The most common deficiency codes reported by the US FDA following clinical investigator site inspections are *Failure to follow the investigational plan* and *Inadequate and inaccurate records*. There has not been any change over time (11).

Ultimately, the biopharmaceutical industry, governments, and regulatory agencies, academic researchers, the medical community, and the media should work collaboratively to fill the gaps and create efficient clinical trial networks and trial designs. A coherent, high-level partnership that brings together key stakeholders on a sustained basis is necessary (12,13).

Over the last decade, many collaborative efforts to transform clinical research have been launched, including:

- the Clinical Trials Transformation Initiative (https://www.ctti-clinicaltrials.org/)
- the European Innovative Medicines Initiative (https://www.imi.europa.eu/)
- the Multi-Regional Clinical Trials at Center of Brigham and Women's Hospital and Harvard University. https://mrctcenter.org/about-mrct/overview/
- the Korean National Enterprise for Clinical Trials (KoNECT), sponsored by the government of South Korea. www.kcc.konect.or.kr
- and most recently Trans Celerate Biopharma: https://transceleratebiopharmainc.com/

Each of these initiatives was specifically designed to address some specific aspects of the clinical trial chain, but no systemic solution has been envisioned.

The need for systems in clinical research and medicines development

The concept of systems, systems approach, and systems engineering have been proposed as possible solutions to address complex problems in public health. Industries other than pharmaceuticals recognized long ago the value and importance of systems thinking and have effectively applied this in their respective domains (telecommunications, transportation, and shipping) with the airline transportation system being the the most representative.

A system could be defined as a set of interacting or interdependent components forming an integrated whole (14). Every system is delineated by its spatial and temporal boundaries, surrounded and influenced by its environment, described by its structure and purpose and expressed in its functioning (15).

Some systems share common characteristics (16), including:

- Structure, it contains parts (or components) that are directly or indirectly related to each other.
- Behavior, it exhibits processes that fulfill its function or purpose; and can be categorized as either fast or strong, as related to its surroundings.
- Interconnectivity: the parts and processes are connected by structural and/or behavioral relationships.
- A system's structure and behavior may be broken down via subsystems and sub-processes to elementary parts and process steps.

The term "systems approach" denotes a methodology applicable to a wide range of science fields. A feature common to all the approaches is their ability to handle data-rich structures of their respective models. The key properties of a system, compared with each of its elements or parts, are its emerging patterns and behavior (17). However, a system's behavior cannot be intuitively predicted by observing each of its components separately or simply summing them up. This explains the needs for simulation-based analysis of models in systems approaches.

Systems thinking has been defined as an approach to problem-solving, by viewing "problems" as parts of an overall system, rather than reacting to a specific part, outcomes or events and potentially contributing to further development of unintended consequences (18). Systems thinking is not one thing but a set of habits or practices within a framework that is based on the belief that the component parts of a system can best be understood in the context

of relationships with each other and with other systems, rather than in isolation. Systems thinking focuses on cyclical rather than linear cause and effect.

Clinical Research in Medicines Development can be defined as an open system involving patients, investigators and associated staff, regulators, sponsors, research sites, and other. as components interconnected through a series of processes aimed to bring effective and safe medicines into the market and maintain them. Because of the above, a *systems approach* is needed to overcome the current barriers to a cost/effective process with appropriate management of the risks involved.

A simple conceptual model of an integrated system for clinical research has been proposed (19) including the creation of ACRES, (Alliance for Clinical Research Excellence and Safety) a nonprofit organization gathering key stakeholders of the clinical research enterprise (www.acresglobal.net) This initiative envisions a global network of high performing research sites interconnected through a shared information technology platform, with standardized policies and operational procedures and a robust, secure database to support mission-critical analysis of performance, quality and safety within an enterprise-wide culture of safety (Figure 1).

The network would operate under the premises of *Accountable Research,* which implies the development, recognition, and acceptance of principles of individual and organizational social responsibility for conducting biomedical research in a manner that assures the interest and well-being of research participants, the safety of therapeutic products, the integrity of all research data and the effectiveness of operational processes to benefit all stakeholders worldwide. Site accreditation

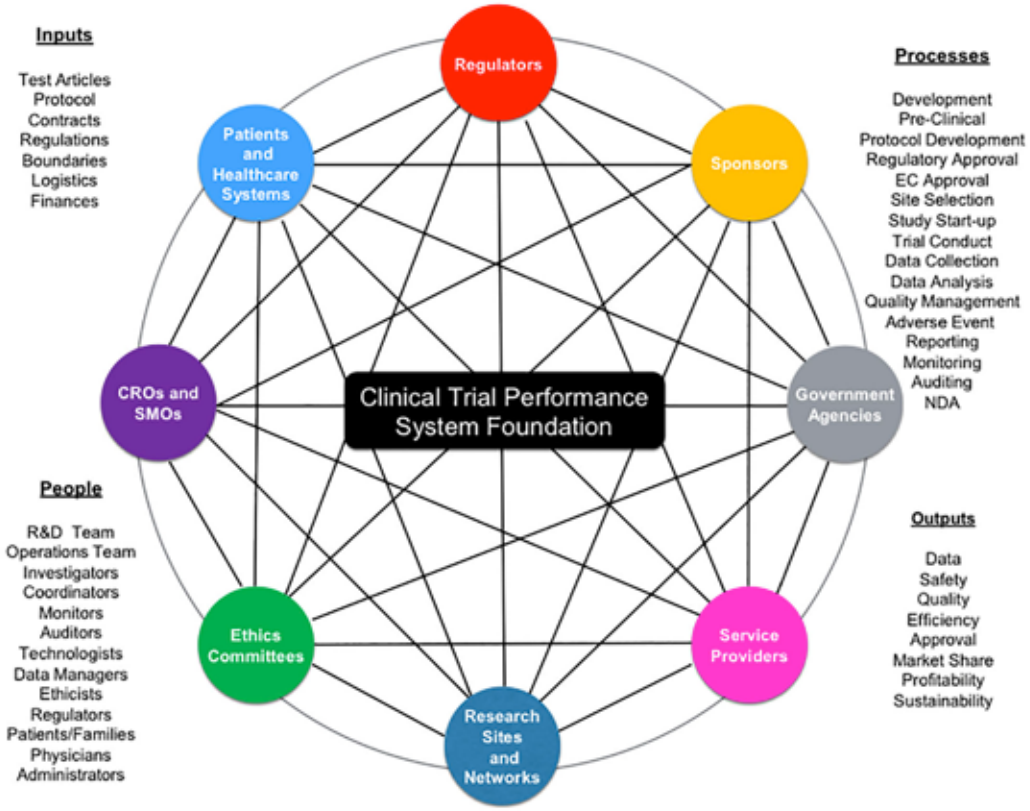

Figure 1. The Proposed ACRES system.

and certification of the clinical research team are key elements for accountable research.

A standard for clinical research site quality management and accreditation

Accreditation addresses the need for a cohesive, effective approach to promoting and sustaining the excellence of clinical research sites while ensuring that such excellence is recognized and rewarded. The costs of conducting clinical trials include inefficiencies inherent in the current process, a process that suffers from a lack of uniform standards, interconnectivity, and interoperability.

ACRES in partnership with the British Standards Institute conceived and incubated the development of the first uniform global standards for clinical research sites through its Site Accreditations and Standards "Initiative" which has now become ACRES' first nonprofit fully independent spinoff - the *Site Accreditation and Standards Institute* (SASI) (https://sasi-accreditation.org/)

The SASI-QMS:2020-1 Standard It is overarching and focused on quality management fundamentals that can assist in creating a culture of competence and conscience that then produces reliable and sustainable compliance. It has been developed to aid the user in assuring the protection of all clinical trial participants and to implement systems and processes to make certain that the results of any clinical trial are valued and valuable. It is intended as the basis for accountability in research wherever, whenever, and for whatever purpose the research is conducted. The standard is available at https://www.sasi-accreditation.org/download-and-read-the-standard/index.html

Site accreditation promotes professionalism and enhances sustainability while reducing cost and time required to effectively evaluate promising products, supports regulatory oversight and compliance, and promotes responsible ethical conduct to make new, safe medicines available to patients more quickly with improved outcomes.

Other ongoing projects developed by specific site accreditation working groups within SASI or as part of the ACRES continuing collaborations with other strategic allies include:

- *Development of a robust* accreditation regimen and protocols for application in conformity assessment to as many 150 000 sites globally. This may require multiple certifying bodies, each of which will require accreditation to ensure the integrity and effectiveness of the conformity assessment process. The Site Accreditation and Standards Institute will be the custodian of the Standard and the process for accreditation.
- *Definition of processes for site recruitment, affiliation, qualification and accreditation*
- *Preliminary classification of sites* including criteria for site selection for potential participation in the various phases of clinical trials (Table 1).
- *Creation of a "universal" developmental model of electronic data flow* mapping clinical trial information exchanges (from trial design through regulatory approval). The project also promotes a comprehensive integration of the model into operational systems at all levels of the health sciences and medicines development enterprise.
- *Secure information exchange using digital signatures*

International expansion, through the appointment of country and regional coordinators, committed to creating awareness of the proposed new system.

Impact, challenges, and opportunities for the proposed system

ACRES was incorporated as a nonprofit organization in 2012 and a favorable reception to the concept, vision, and goals among critical stakeholders among regulatory agencies, pharmaceutical companies, academic sites and lay public was observed. A steady influx of strategic allies willing to partner in achieving the ACRES vision followed.

However, five major obstacles or barriers to entry have been identified:

1. Conceptualization of the system and its parts
2. Accepting the feasibility of building such a system
3. Visibility and clarity of the ACRES message

Table 1

Minimum criteria for site qualification

Parameter	*Site Level I*	*Site Level II*	*Site Level III*	*Site Level IV*
Studies conducted	PMS/PASS/ Comparative Effectiveness	Phase IV or Phase IIIb	Phase II-III Investigator-Initiated	Phase I-III IIS
Study endpoints	Patient-Reported Laboratory Surrogate Markers	Level 1 + Novel Biomarkers	Level 2 + Not validated biomarkers	Level 3 + Exploratory biomarkers
Number and complexity of Procedures/Protocol	Few	Intermediate	High	High/very high/Proof of concept
Expected Safety Profile	No specific safety issues/ Well known AE profile	Level 1 + Unknown SAEs	Level II + Unknown AE/SAE	First in humans Unknown SAEs/AEs
Study duration Patient demographics	Days to months Outpatients	Weeks/Months Outpatients/ Inpatients	Days to Months Outpatients/ Inpatients	Days to Months Out and Inpatients
Average # of studies conducted/year	<5	<10	<15	15
Site technological facilities	Few; Standard of care	Few; Standards of care	Level II + advanced technologies	Advanced technologies genomics
IT communication facilities	Acceptable	Acceptable	Good	Excellent
Expertise in diverse medical Ssecialties	Single disciplines	2-3 medical	Several (5-10)	>10
GCP compliance in the past 5 years	<1 audit	<3 audits and no critical audit findings	< 5 audits and no critical audit findings	>5 audits and no critical audit findings
Investigator and staff certification	No	No	Yes	Yes
Emergency medical care available	No	Yes	Yes	Yes

Adapted from: Silva H, Koski G, Whalen M, Tobin M, Widler B, Pacino AO, Edwards B. A systems approach to enhance clinical research and medicines development. J Med Develop Sci 2015. Dx.dooi.org/10.18063/JMDS.2015.01.004

among and across the stakeholders

4. Resistance to change among well-established groups
5. The continued need to generate sufficient resources, both financial and in-kind assistance, to support mission-critical

initiatives and the basic ACRES infrastructure even though most of the work is done through volunteerism.

On the other hand, multiple initiatives could be competitive or overlapping. This could lead to ACRES being perceived as redundant/ unnecessary. ACRES' goals and strategies should be clearly articulated in the community. Further distinctions between ACRES and other initiatives are needed.

Some attempts to overcome the above-mentioned barriers have been devised and thus the systems concept has gained gradual support within the research community. Furthermore, some of the initiatives have been already adopted (or adapted) by specific stakeholders as part of their respective operations (but not as part of the intended system). However, the resistance to change is well embedded.

ACRES has also worked diligently to establish a relationship with the world's regulatory agencies in the USA and Europe as well as with big pharma and global professional associations since the failure to receive endorsement and acceptance by these groups would be critical for the sustainability of the purposed system.

The implementation of ACRES purposed system will indeed require a complex and challenging path and significant obstacles are anticipated. However, the realization that this is the best long-term option among stakeholders and the public is a powerful incentive for the ACRES contributors and strategic allies to keep working on a volunteer basis to make it happen.

Needs for education and training in clinical research and medicines development: Role of professional competencies

The lack of an adequately sized and appropriately trained multi-professional workforce both in the industry-related and the academic clinical research field is also a significant part of the problem. Competent professionals (pharmaceutical physicians, clinical investigators, and other biomedical professionals) would be much better able to perform effectively in their specific responsibilities in bringing and maintaining new medicines in the marketplace.

The root of the problem resides in the lack of proper education in clinical research and medicines development (also known as pharmaceutical medicine) at the undergraduate and postgraduate levels across academic institutions involved in educating biomedical professionals worldwide. The involvement in clinical research and/or working in pharmaceutical medicine has been perceived as a task and not as an element of the profession. Most professionals are trained "on the job" and this lack of education is conducive to a lack of professional identity among most biomedical professionals working in this area of healthcare.

Medicines development has gradually become a compartmentalized and segmented activity and gradually the focus has been made on education and training for the individual compartments or domains safety, regulatory, clinical research, medical affairs, health outcomes. However, the principles of pharmaceutical medicine as a discipline and a professional activity are fundamental to ensure a proper balance in meeting the needs of the health-care system, the patient, the regulatory agencies and the pharmaceutical industry. Therefore, a professional involved in medicines development should be able to master all of the competencies needed for effective performance.

Competency-based education (CBE) is an emerging discourse in the health profession's education and has been adopted by numerous academic institutions and professional associations all over the world, at the undergraduate, postgraduate and continuing professional development (CPD) levels (20).

Competencies refer to the "observable ability of a health professional to integrate knowledge, skills, values, and attitudes" to perform effectively. *Competencies* are the ingredients of *Competence*. A competent professional is the one possessing the required abilities (competencies) in all domains in a certain context at a defined stage of education or practice. The progression of competence, from novice to mastery, can be also defined (21).

A working group was formed within IFAPP (International Federation of Associations of Pharmaceutical Physicians and Pharmaceutical Medicine; www.ifapp.org) including

representatives from PharmaTrain, (a network of academic institutions and private partners sponsored by the European Union Innovative Medicines Initiative charged with the creation of standards for education in pharmaceutical medicine www.pharmatrain.eu), with special interest and experience on Quality Improvement through education. A basic set of 7 domains and 57 competencies and a Statement of Competence were defined (22). The competencies were aligned with the learning outcomes of the base course offered by PharmaTrain and thus a standard for competency-based education (at the cognitive level) is currently being used for certification, education, and training by the organization and the IFAPP Academy, its educational arm (www.ifappaacademy.org) (Table 2).

More recently, another IFAPP sponsored working group developed the full set of applied knowledge, skills, behaviors, and attitudes for each competency (23). A process for internal and external validation with the Entrustable Professional Activities (also called Capabilities in Practice) has been initiated by the General Medical Council and Academy of Medical Royal Colleges of the UK.

Pharmaceutical physicians (PPs) and medicines development scientists (MDS) need a certain level of competence, achieved through a postgraduate education foundation, on-the-job experience, and continuing professional development programs. To assess the self-perception of competence, education, and training needs, an on-line questionnaire based on the seven domains of competence, developed by IFAPP-PharmaTrain, was prepared and distributed among PPs and MDS members of IFAPP's affiliated professional associations in countries with facilities for

Table 2

Statement of competence

The Pharmaceutical Physician/Drug Development Scientist:

- Is able to identify unmet therapeutic needs, evaluate the evidence for a new candidate for clinical development, and design a Clinical Development Plan for a Target Product Profile.
- Is able to design, execute, and evaluate exploratory and confirmatory clinical trials and prepare manuscripts or reports for publication and regulatory submissions.
- Is able to interpret effectively the regulatory requirements for the clinical development of a new drug through the product life cycle to ensure its appropriate therapeutic use and proper risk management.
- Is able to evaluate the choice, application, and analysis of post-authorization surveillance methods to meet there requirements of national /international agencies for proper information and risk minimization to patients and clinical trial participants.
- Is able to combine the principles of clinical research and business ethics for the conduct of clinical trials and commercial operations within the organization.
- Is able to appraise the pharmaceutical business activities in the health care environment to ensure that they remain appropriate, ethical, and legal to keep the welfare of patients and participants at the forefront of decision making in the promotion of medicines and design of clinical trials.
- Is able to interpret the principles and practices of people management and leadership, using effective communication techniques and interpersonal skills to influence key stakeholders and achieve the scientific and business objectives.

Adapted from: Silva H, Stonier P, Buhler F, Deslypere JP, Criscuolo D, Nell G et al. Core Competencies for pharmaceutical physicians and drug development scientists. 2013. Front Pharmacol 4:105 doi 10.3389/fphar.2013.00105

postgraduate education. The data collection was run over a fixed period of three months in Japan, Italy, Brazil, and Spain during 2017. Results indicate low but variable levels of perceived competence for the various domains as well as seniority in the job. All respondents declared a significant need for continuing professional development in all domains (24).

These results corroborate and support the continuous efforts, put in place by IFAPP and the IFAPP Academy to foster the development of accredited education and training among professionals involved in medicines' development.

The competencies are intended to serve as a resource and guide for those interested in improving the quality and accountability of pharmaceutical medicine education and training. The model may foster further granularity and thus specific sub-competencies and specialty competencies that apply to specific functions in clinical research and drug development could be identified. The primary vision for this competency model is to facilitate the availability of professionals more fully prepared for the ongoing challenges and opportunities in medicines' development.

Competency-based profiles of key jobs in medicines' development can be effectively devised. Standardized job descriptions for various functions could be developed globally. Additionally, it would provide reassurance to stakeholders of the drug development process that it is in the hands of competent people who are measured against a set of performance standards.

Competency models are iterative processes, and the model will have to be regularly updated as the competencies are deployed and used for professional, academic, or self-assessment purposes, and the business and scientific environments evolve.

Competencies in clinical and translational research. Professional workforce development

Clinical and translational research is the stage of medicines' development that is conducted on human volunteers. It is one of the most resource-intensive and most highly regulated components of the medicines' development process. It is widely agreed that there has been a significant increase in both the number and complexity of clinical trials during the past decade. The professionals that participate in clinical and translational research include principal and co-investigators, clinical research coordinators, clinical monitors, data management professionals, regulatory affairs professionals, and many research and project managers. The demand for clinical research professionals (CRPs) already exceeds the supply and the pressure to increase the size of the pool of competent CRPs will undoubtedly continue.

Currently, there is no required educational background or defined set of competencies that are necessary to become a CRP. Most of the current workforce has been trained "on the job". Very few enter the clinical research profession as a direct result of undergraduate education or knowledge of the field (25). Onboarding training in clinical research is typically minimal or poorly organized (26).

Three professional organizations certify CRPs, but none requires educational preparation, only experience, and the passing of knowledge-based (not necessarily a competency-based) examination. Although certified CRPs are generally regarded as having higher levels of competency, the shortage of CRPs is only exacerbated by the "Catch22" situation of needing the experience to get a job and professional certification but needing a job to get experience and professional certification. Not only does the clinical research workforce solution require an influx of new competent professionals, but it requires the current workforce to continually enhance their competency through professional development activities.

As the concept of competency-based education and training has spread to the clinical and translational research enterprise, many groups have produced lists of knowledge, skills, and attitudes, which define the core competencies required for many of the specific roles within the enterprise. In 2013, a broad-based and widely representative group including representatives from pharmaceutical companies, contract research organizations, academic institutions, clinical research sites, and professional societies was hosted under the auspices of ACRES (Alliance

for Clinical Research Excellence and Safety), MRCT (Multi-Regional Clinical Trials at Harvard University), and ACRP (Association of Clinical Research Professionals). Members of this group formed the Joint Task Force for Clinical Trial Competency (JTF) which agreed to work toward aligning and harmonizing the many role-focused statements relating to core competency 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. A total of 51 competencies distributed among eight domains were agreed upon and a Core Competency Framework (CCF) was defined (26) (Figure 2). Subsequent efforts of the JTF have incorporated competencies related to project management as well as defined the competencies at the levels of Basic, Skilled, and Expert to recognize the increase in competency which occurs as a CRP gains experience in the field (27). The JTF is housed within the Multiregional Clinical Trials Center of Brigham and Women's Hospital and Harvard and maintains a continually updated website at https://www.mrctcenter.org/clinical-trial-competency.

In 2016, JTF conducted a global survey designed to assess the level of competency of the current CRP workforce and to inform the needs for education and training necessary to enhance the performance quality of their roles. The responses were grouped by role within the clinical research team (Principal Investigator, Co-Investigator, Research Nurse, Study Coordinator, etc.). The results suggested that irrespective of the role or the time functioning within the clinical research enterprise, there were lower levels of competency in the domains of "Scientific concepts and research design" and "Medicines development and regulation" (28). These results

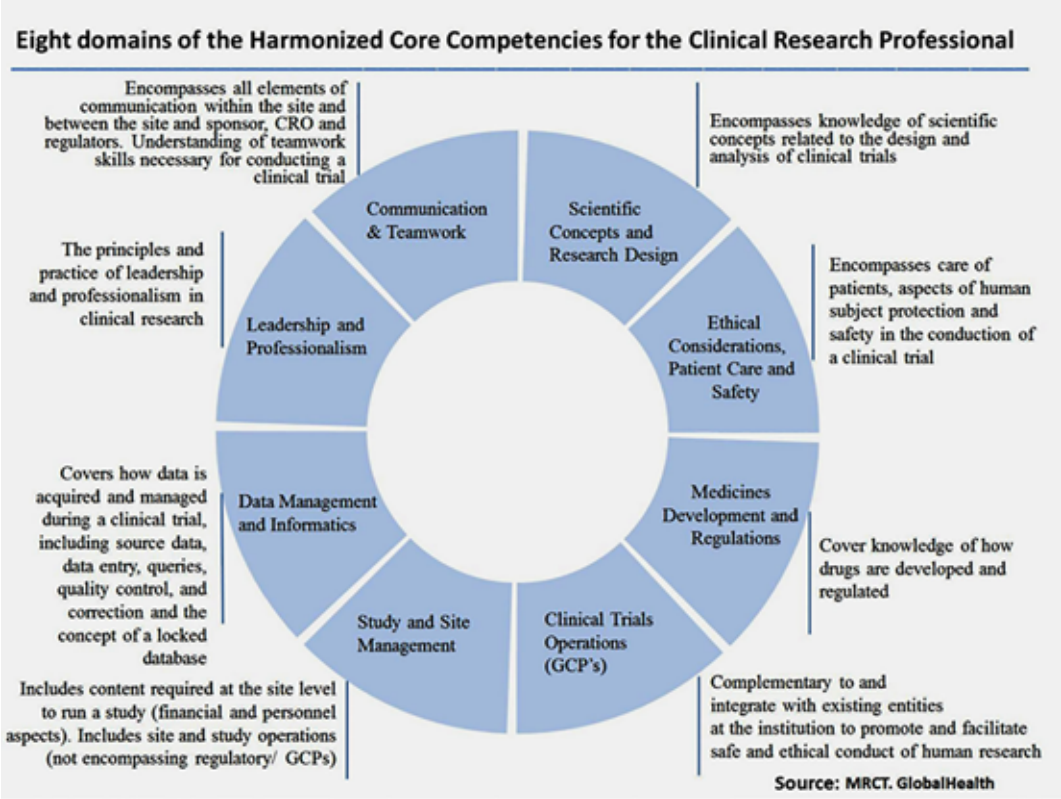

Figure 2.

confirm previous findings in Latin America (29).

The JTF CCF has been widely recognized as the Standard for education, training, and professional certification globally by professional organizations representing CRPs and by academic programs that educate CRPs. The JTF CCF has been used to inform on boarding by corporate entities and by clinical sites to create their job descriptions.

CONCLUSIONS

It is apparent that in today's clinical research enterprise growing rapidly in size and complexity the time-honored "learning on the job" is no longer sufficient to produce a qualified clinical research professional and ensure proper conduct of clinical and translational research and protection of human participants. Basic education in the medicines development process and enhanced education and training in the clinical research domains is required. While all domains should be included in curricula, increased content that focuses on "Scientific concepts and research design" and "Medicines' development and regulation" is indicated.

Despite the growing awareness of competency-based education and the need for implementation of systems-thinking among the various stakeholders involved in medicines' development, its full adoption is still on the horizon. Resistance to change is one of the obstacles to overcome. Continuing efforts to creating further awareness and the various scenarios needed to developing better medicines are key responsibilities of the professional associations and academic institutions involved in drug development.

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