The Clinical Trials Landscape: Limitations, Strengths, and Promise

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The viability of clinical trials in the U.S. depends upon the strength of the academic health center infrastructure

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UNDERSTANDING THE LANDSCAPE

The complex infrastructure that creates and sustains clinical trials in the U.S., specifically the systems established within the nation's academic health centers to conduct and implement clinical trials in response to patient needs, scientific demands, and national concerns, is little noted and rarely studied. Clinical trials are clearly recognized as a significant component of America's research enterprise and a critical element of America's preeminence in science worldwide. These trials, research studies carried out with human volunteers to answer specific questions concerning the effectiveness of a drug, device, treatment or diagnostic method, are designed to advance scientific knowledge and promote discoveries to treat and cure illness and disease, and increase longevity and the quality of life for countless people.

Clinical trials administration and compliance at academic health centers nationwide has been rapidly changing in recent years as a result of increased research activity, mounting regulatory requirements, and escalating costs. As new infrastructure emerges, the current administrative landscape for clinical trials requires assessment to: (1) recognize the complexity and identify the inter-dependencies of clinical trial compliance with all major functions of academic health center operations; (2) analyze the strength of academic health center clinical trial compliance resources; (3) harmonize operations and functions; (4) determine both essential business requirements and future technology solutions; (5) ensure that the compliance infrastructure responds to the current regulatory environment and; (6) ensure the future viability of clinical trials for the nation.

Ultimately, the administrative infrastructure is linked with the sustainability of the nation's research enterprise and the health of the public. National spending on clinical trials was approximately $25.6 billion in 2006, and projected to increase to $32.1 billion in 2011. The global

clinical trials industry is worth an estimated $10 billion, with the potential for considerable future growth. The impact of clinical trials on health is incalculable.

THE KEY ELEMENT OF THE LANDSCAPE: CLINICAL TRIALS BILLING

Key to understanding the strengths and limitations of clinical trial compliance systems is the clinical trials billing processes, considered to be the most complex and problematic aspect of clinical trials administration. The authors of this paper profiled the clinical trial billing processes at 15 academic health centers in late 2006 and early 2007. Private and public institutions were selected and institutional profiles developed through telephone interviews with chief compliance officers who described clinical trial billing processes and organizational structures as well as current challenges and institutional transformations underway. Officers described the methods and systems used to enroll, track, register, and bill patients in clinical trials and best practices within the institution. The observations from these initial profiles were later validated by information from another set of chief compliance and administrative officers in the Forum on Regulation of the Association of Academic Health Centers.

This assessment was needed and timely given the rapidly changing landscape of clinical trials compliance as institutions seek to improve and enhance systems to serve patients nationwide.

OBSERVATIONS

Organization, Governance, and Structures: Decentralization Reigns

Decentralization characterized the various functions related to clinical trials in the majority of institutions. Governance and infrastructure were not always complementary given that two, three, or even more legal, professional, or research corporations could exist within the academic health center.

Thirteen of the 15 profiled institutions reported decentralized structures for clinical trials compliance, due in part to real or perceived organizational and governance barriers as well as turf issues. Only two institutions had consolidated all functions into one office although all institutions reported consolidation underway in some form or another.

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Tremendous disparity in procedures, operations, and approaches to clinical trials operations and management was evident. Major technological barriers and operational fragmentation hampered the creation of common structures and systems.

Labor-intensive manual operations characterized clinical trial operations, particularly in the billing realm, with a large number of critical operations performed by hand in a majority of the profiled institutions. Invoicing and tracking of payments from sponsors, for example, relied heavily on manual interventions.

The capabilities to track all enrolled clinical trial subjects across the institution did not exist at any profiled institution or a centralized office for tracking study patients or their study-related appointments.

In response to these shortcomings:

- All profiled institutions were upgrading or developing new software to better track patients and improve billing systems.
- A majority of institutions were establishing data bases to manage information on clinical trials subjects in the clinical trials offices.
- Institutions were making major changes in the monitoring of patients enrolled in clinical trials (see fig. 1).

Leadership

Varying degrees of senior level management support and leadership were noted at profiled institutions. Organizational issues, including differing agendas and lack of alignment on compliance priorities for health professional

schools, hospitals, and practice plans often accounted for such differences. Nevertheless, senior level management was increasingly engaged in planning or directing institutional change in clinical trial administration and compliance.

Management Systems

Clear, focused management controls or demarcated check points along the continuum of the clinical trial process—from the study design to the close-out of the trial—were not evidenced in most profiled institutions. The clinical trial roadmap for operations was rarely defined or managed by policies or procedures; instead, people fulfilled various functions based on individual connections and communications established over time.

In decentralized systems, in particular, 20 different areas of operations where personnel were involved in clinical trials billing processes could often be identified. The lack of systematic check points to ensure timely control and compliance was a major factor leading to an oversight system based on manual operations that were very much positioned at the back end of operations.

Given that the functions to fulfill the clinical trials objectives varied enormously within and among institutions, chief compliance officers did not always have a clear or accurate picture of the totality of clinical trial operations (e.g., number or type of clinical trials, range of research activity and/or volume within departments or across the institution, program or personnel costs).

These management deficiencies were often exacerbated by tremendous staff turnover reported at many profiled institutions.

Consolidated Business Practices

Consolidation of functions and activities is occurring but no uniform or standard structures or guidelines for change have emerged. Consolidated business practices and processes appeared to be lacking. This inability to optimize business activities resulted primarily from the lack of robust IT solutions that could provide comprehensive and integrated data collection capabilities. This exposure from inadequate or imperfect data made it difficult, if not impossible, to effectively reengineer business processes.

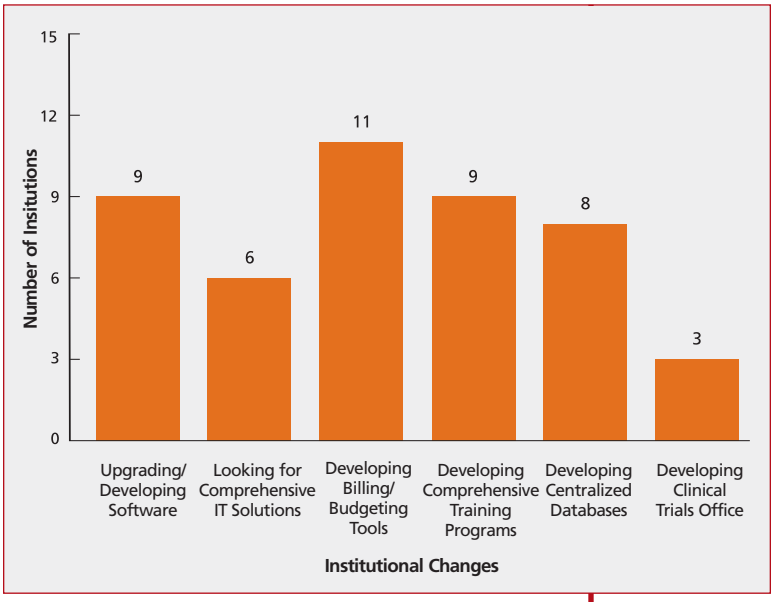

Fig. 1. Institutional Changes in Clinical Trials Administration

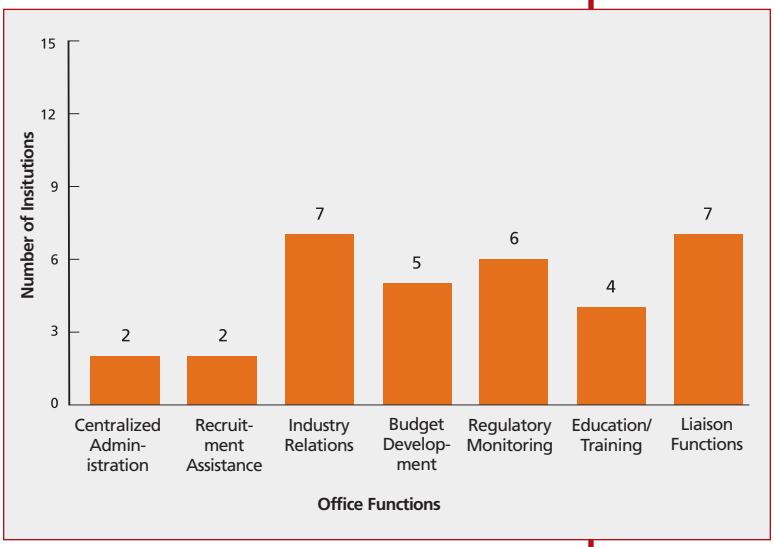

Fig. 2. Functions of Clinical Trials Offices

Consolidation was most often evidenced by the establishment of a clinical trials office, with eight of the profiled institutions establishing such an office (see fig. 2). Of the seven institutions where a clinical trials office did not exist, three reported plans to establish such an office. Clinical trial operations were divided among four to six administrative areas in those institutions without such an office.

While clinical trials offices were becoming a clinical trial hub, no uniformity in structure, operations, or responsibilities was found. Of the eight clinical trials offices, two operated as a control point for clinical trials and served as gatekeepers for paperwork associated with clinical trials; another two offices had responsibilities to assist research personnel in recruiting and enrolling patients in clinical trials; four offices offered educational and training programs for researchers; and seven offices were the liaison between researchers and the hospital.

Seven offices had responsibilities to support clinical investigators in the conduct of industry-supported clinical trials (e.g., searching funding opportunities, negotiating and/or drafting clinical trials agreements with sponsors, liaison between the researcher and the sponsor). Five offices provided financial expertise to clinical investigators from protocol development to budgeting, cost analyses, and prospective reimbursement analyses.

Six offices served as a monitoring body, monitoring and/or auditing projects for compliance with the sponsor's terms and conditions, university policies, and federal regulations.

Staff Competencies

Institutions lacked depth in terms of staff with the professional skills and competencies required to fill key administrative positions that would fully address institutional clinical trials billing operations.

Communication and Education

No formal communication infrastructure for clinical trial compliance activities existed at any of the profiled institutions, thus hampering activities that were already labor and effort intensive. Again, adequate check points to ensure communication and education along the continuum of the clinical trials processes were lacking. Communication was often via website postings of institutional policies and procedures and federal regulations.

Educational programs were viewed as the panacea for breaking down communication barriers between the compliance and research functions. Institutions cited a multitude of educational and training programs from web-based orientations on clinical trial policy to face-to face training on Health Insurance Portability and Accountability Act (HIPAA) and institutional review board (IRB) compliance, which were offered to researchers, study coordinators, and other staff with diverse educational backgrounds and technical skills. Eight of the profiled institutions offered access to a certification program (e.g., certified clinical research coordinator) for study coordinators.

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All institutions had instituted new communications strategies and educational programs to improve communication between research and billing staff, often cited as a major challenge. Another challenge was ensuring consistent involvement of principal investigators (PIs) in educational programs.

Training on billing compliance was only offered by five of the profiled institutions. Four institutions posted a manual of billing procedures online and nine posted other information, including budgeting templates and worksheets.

Interestingly, when clear channels of communication did exist, particularly between hospital billing staff, research coordinators, PIs, and other research personnel, compliance administrators reported that staff morale increased along with perceived or real increases in efficiency and effectiveness.

Information Repositories

A centralized data repository (serving as the single source of informational knowledge) from which any stakeholder can access essential business activities (i.e., costs, resources, volume, and sources of trials) was lacking in all profiled institutions although many institutions reported plans to create such repositories in the near future. Many compliance officers expressed doubt that such an effort could be achieved in the next five years given the increasing costs of compliance.

Enrollment, Tracking, and Billing

Difficulties in tracking research participants were reported in all profiled institutions; tracking was deemed to be the responsibility of the principal investigator's department in most profiled institutions. The lack of alignment between medical school/research and hospital registration systems for identifying research patients and their associated charges was evident, which created an inefficient encounter-driven system that relied on manual intervention that could pose institutional risk at all stages.

Web-based software does not currently exist to permit the university and hospital financial programs to interface, which accounted in large measure for the inability to track all enrolled subjects (see fig. 3). One institution reported tracking patients by using an Excel-based program supported by a shared drive IT model. However, compliance officers reported that such an approach was neither desirable nor sustainable for the long-term.

Although study-related appointments were not tracked campus-wide, one institution did have a central-source system, which captured and tracked all study participants by study/PI from enrollment to billing close-out, and currently permitted the central tracking of 600 enrollees.

Billing offices often did not have a clear idea of what data elements were required and at what point they were needed for billing. Each department handled billing differently and billing analysis/worksheets varied across institutions. Billing complexity, varying payer requirements, decentralization, and unclear regulatory guidance were reported as compounding billing challenges.

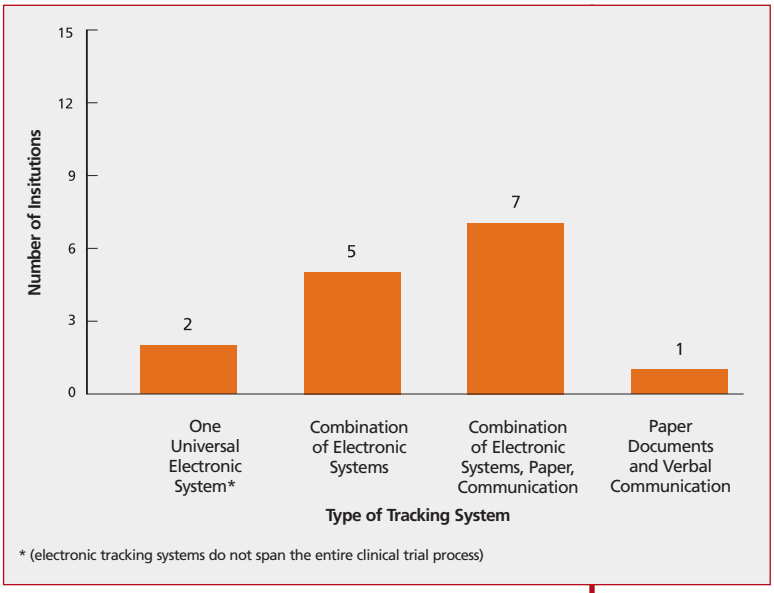

Fig. 3. Tracking Systems for Patients Enrolled in Clinical Trials

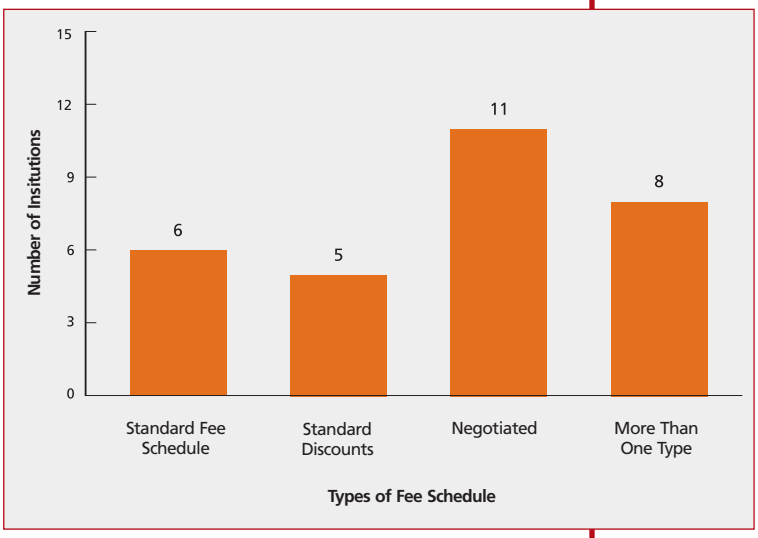

Fig. 4. Fee Schedules for Research Services for Clinical Trials

Budgets and Fee Schedules

Often 200-300 study coordinators throughout the institution were involved in developing budgets. Nevertheless, the development of a budget with up-front prospective budget analysis was viewed by all compliance officers as the key control point for all tracking.

Institutions did not appear to have clear decision trees, including fiscal review processes, for developing fee schedules. Almost every institution reported having a coordinator in many, if not all, departments of the medical school with major responsibilities for obtaining fee schedules for services. Departmental coordinators in nine of the profiled institutions also had responsibilities for negotiating fee schedules.

Neither one model nor one process for delineating responsibility in fee negotiation was evident in the profiled institutions or emerged as a front runner for replication in other institutions. Only six of the profiled institutions had established a standard fee schedule for research related services (see fig. 4).

IT Systems

Every profiled institution cited the inability of hospital and/or clinic billing systems to interface with university systems related to the research study. A multitude of systems existed within the profiled institutions (see fig. 5). Homegrown, and often less than satisfactory IT solutions, were reported; everyone hoped that the IT industry would be able to provide appropriate products for the future.

It was significant that hospitals did not, or on rare occasions, conducted annual policy assessments to ensure that their computer systems evolved in sync with the organizational changes occurring within the hospital or the academic health center.

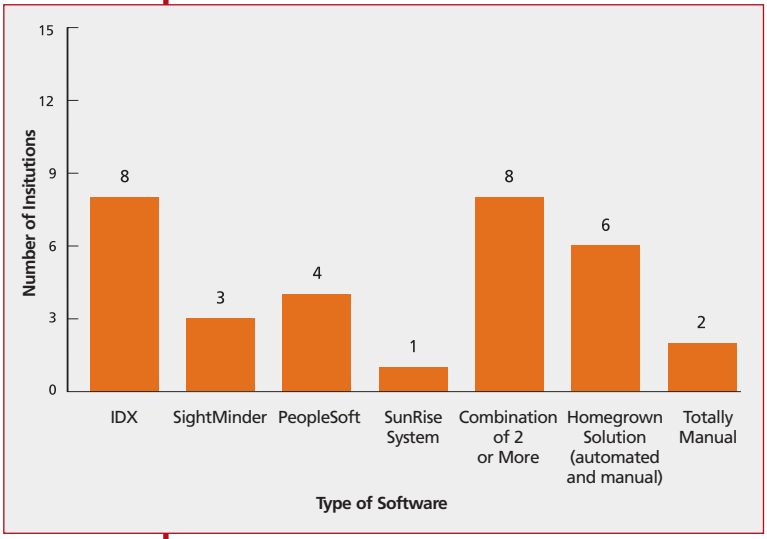

Fig. 5. IT Use in Billing for Clinical Trials

POINTING THE WAY TO STRATEGIC IMPERATIVES

These observations highlight the stresses and challenges within the clinical trial infrastructure. More important, they provide a baseline to assess the current operational environment at academic health centers, to delineate the impediments to progress, and to suggest the agents of change that should become the strategic imperatives to ensure improvements in clinical trial operations and, thus, in the nation's research agenda.

The 12 strategic imperatives that will create the new landscape for clinical trials:

- Academic health centers will need to define a centralized/consolidated clinical trial governance structure and organization that aligns organizational commitment to operations.
- Policy will need to be developed and enforced by the top institutional leaders who are perceived as key figures in raising awareness about the complexity of compliance and advocating for needed changes and improvements.
- Academic health centers need to develop functional process maps that define principles and define the roadmap for all stakeholders in the compliance process related to clinical trials.
- Integration of a comprehensive IT automated solution is essential. The functional process map leads to a business requirements document that is essential for developing an IT solution.
- An assessment of needed personnel skills and competencies must be conducted to ensure that institutions are adapting to changing regulatory and business requirements.
- A single source of information with the costs, resources, volume, sources of trials, and impact of an institution's clinical trials is needed.
- Expanding educational offerings, specifically with an emphasis on billing compliance, is essential to ensure successful operations.
- Ensuring effective communication with all clinical trials personnel, particularly principal investigators, is key to successful system operations and essential to enhance understanding about the importance of consistent policies and practices.
- Increased standardization across institutions with regard to clinical trials management systems and business process activities must be consistent, operationally practical in design and execution, and synchronized across all key stakeholder functions.
- Academic health centers must foster closer relationships with local fiscal intermediaries to establish and strengthen both business process and organizational alignment for clinical research billing activities.
- Academic health center-hospital relationships must be nurtured with regard to clinical trials,

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for the effectiveness and success of a program depends on how clinical sites treat, care for, and bill clinical trial subjects.

- Academic health center leaders should open a dialogue on different approaches to fee schedules according to the funding source, recognizing that fee schedules need to be realistic, competitive, and rationale. Fees that are simple and accurate, clearly defined, periodically reviewed, and have the support of all institutional leaders are essential.

These strategic imperatives recognize the following:

Organization, Governance, and Structure

Traditional dysfunctional processes need to be abandoned and replaced by centralized policies and a shared vision agreed to by all stakeholders.

Establishing a centralized clinical trials office to perform cost analysis, prospective reimbursement analysis, and other financial services is a first step in ensuring consistency and efficiency in operations as well as limiting the number of technical subject matter experts needed throughout the institution.

Academic health centers will need to organize their clinical trial requirements by functions across the institution (e.g., research organization, proposal development, budget development, system interfaces) and business requirements will need to be prioritized (i.e., essential, core, desired, preferred) within each functional area.

Leadership and Management Systems

A major challenge for all academic health center leaders will be to balance the stewardship of an institution that has a governance structure that appropriately maintains compliance oversight with the management of an administrative infrastructure that is suitable and realistic from the perspective of the PI who must work within the system. Management controls and auditable check points along the clinical trial continuum will need to be designed to focus on efficiencies, facilitating operations, and compliance concerns. These controls should be directed first at high risk areas to minimize institutional vulnerabilities.

Academic health center leaders are key players in strategic planning and policy development, which should include development of a functional process or roadmap, a business requirements document, and evaluation mechanisms. To address the increasing costs of compliance, leaders will have to open an informed dialogue with research sponsors to ensure that true, fully-loaded costs are covered in clinical trials.

Academic health center leaders should consider addressing questions related to the development of standards within and across institutions and working collectively to establish a uniform methodology in the design, assessment, and evaluation process for clinical trials management system solutions for academic health centers nationwide.

A clinical trials management system should be used to calculate costs and track patients for projects, regardless of funding source (e.g., industry, foundation, federal). Such a system must also be able to interface with the data warehouse for reports and account for the various administrative/management functions and events, including: administrative and pre-budgeting set-up, budget preparation and negotiations (both internal and external), research award notifications, accounts set-up, study management, study close-out, and other general reporting requirements.

Functional Process Map and Consolidated Business Practices

The functional process map (see fig. 6), which not only describes the activities and tasks spanning clinical trials administration but also reveals stakeholder involvement at all points, is a forceful tool developed to assess the institutional environment for clinical trials, critique current processes and gaps, and prioritize areas to address.

This roadmap can reveal where institutions can increase effectiveness, create efficiencies, and ensure success in clinical trials administration. Ultimately, the map can lead institutions to consider the skills and competencies of needed personnel, the associated business requirements to support the operational checks and balances with clinical trials

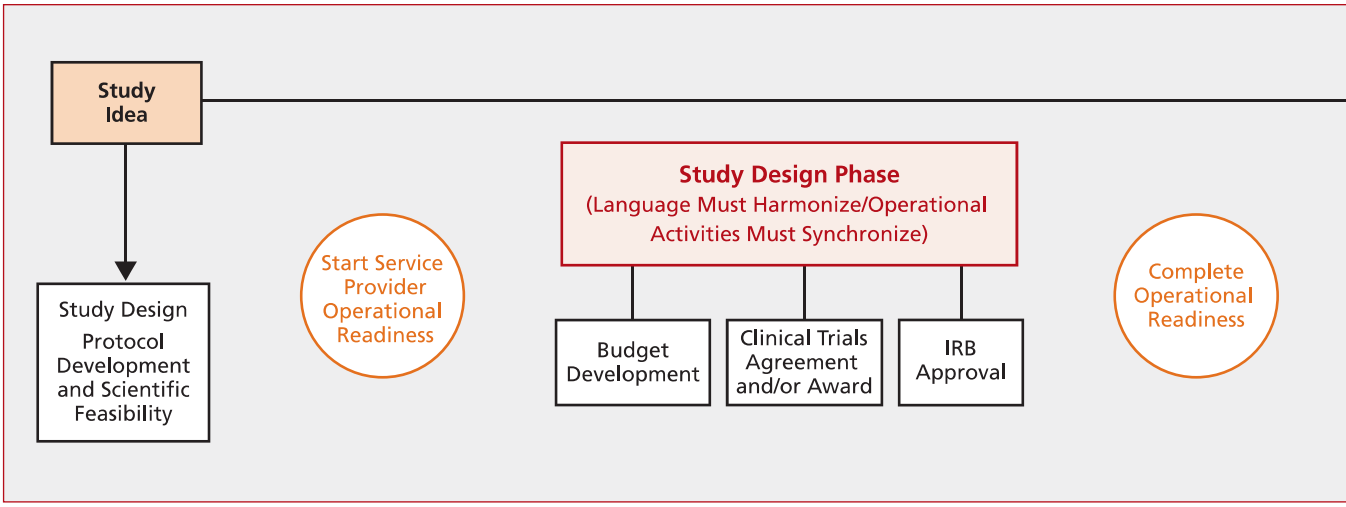

Fig. 6. Clinical Trials Functional Process Map

billings, and specific IT requirements to ensure program advancement and sustainability.

In building a functional process map, key stakeholders from leadership to personnel in all the functional areas involved with clinical trials (e.g., PIs, research administration, general counsel, deans) must be included.

Staff Competencies

An assessment of skills and competencies establishes mandatory qualification requirements for selected job classifications as well as appropriate guidelines and incentives to recruit and retain personnel with such requirements.

Education and Communication

Both practical and credential-oriented educational offerings should be established to help support the clinical trial compliance program and to build a culture of accountability. It is imperative that educational offerings are structured to resonate with various key stakeholders in the process and include an evaluation process that ensures that learning has occurred. New ways to engage PIs and other research personnel in compliance issues are necessary for the future. Building self-reliance in all stakeholders so they can navigate any and all aspects of institutional requirements to effectively advance clinical trials with the organization's support should be an educational goal.

Enrollment, Tracking, and Billing

With increased standardization, the research and compliance communities within academic health centers can concur on best practice models that should be exported to institutions nationwide.

Academic health centers will need to provide the hospital component of the institution with tools and/or information that clearly define the hospital's investment in the research mission to ensure involvement and collaboration on clinical trial billing issues. As relationships with affiliated clinical sites are very complex, leadership teams should be involved throughout any change process.

Budget Development and Fee Schedules

Institutions should strongly consider transitioning from budget development by a multitude of study coordinators to one central office within the academic health center.

Institutions should develop the rationale and justification for existing fee schedules. To ensure administrative simplification and fairness, one fee schedule should be determined within a set timeframe. Given the pace of change related to

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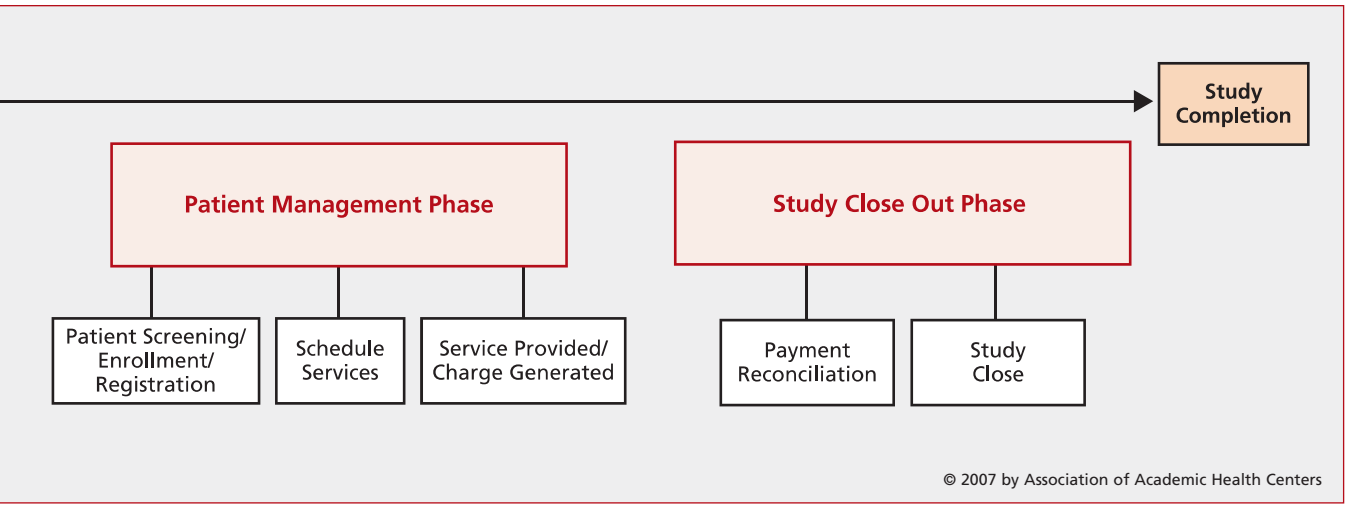

clinical trials, a two-year timeframe should be considered for this task.

Ultimately, academic health centers need to commit to standardized fees schedules in the near term and should establish processes to move toward one fee schedule for the future.

IT Solutions

The IT solution must bridge both academic and hospital activities and be a "start to end" solution that enables operational uniformity and transparency. Such a solution will particularly eliminate errors in the clinical trials billing process that result from the current manual system.

The institutional functional process map, which leads to a business requirements document, is essential for developing an IT solution. By using institutional functional process or road maps, the academic health center community will be able to define the data systems and software needs of the research community to potential IT providers as well as influence IT solutions in an IT market that is still immature in its offerings related to clinical trials.

CONCLUSION

Clinical trials administration and oversight require the fullest attention of academic health center leaders. Academic health centers are at a nexus between the past and the future, and have a pivotal opportunity, if not obligation, to provide an enhanced infrastructure that facilitates but does not hamper or over manage the critical work of discovery and scientific innovation. Successful management of clinical trials along with administrative simplification that results in efficiency and proactive rather than reactive behaviors related to research and compliance can be fostered as academic health centers increasingly move toward and adhere to mutually agreed upon guiding standards.

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