DEVELOPING NEW PATHWAYS FOR CLINICAL RESEARCH THROUGH THE CHANGING ENVIRONMENT OF 21ST CENTURY HEALTHCARE

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The increasingly high costs of performing clinical research through the established “university-academic” model have become increasingly recognized. Most specifically, in the area of federal and other foundation-sponsored “granted” trials, the gap between the “real costs” of research and the actual dollars “granted” to perform such trials are becoming increasingly disparate. Therefore, the ability of research centers, especially newer centers, to significantly enter and compete in the research arena is becoming more and more difficult. Even longstanding university-academic centers are finding it harder and harder to cover the full costs of financing such research under this system. The evolving model of industry-sponsored, pay-for-performance clinical trials can offer potential solutions for entry into and support of clinical research structures without the extensive overhead and indirect costs usually associated with “granted” trials. This model also allows nonacademic hospitals an opportunity to enter into the clinical research marketplace and may additionally serve, in an era of increasingly RVU-driven clinical practice environments, as an alternative recruitment and entry point for the expansion and encouragement of a cadre of new “physician-scientists with a medical degree,” a group that the NIH has defined as an “endangered species.”

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The high cost structure related to the “academic-university” model of research has been accurately discussed in the recent article by Holbrook and Sanberg (7). This model, developed in the latter half of the 20th century, supported and dominated by the federal government via programs such as the NIH and NSF, has been the leading academic-university research model in the US over that period of time.

However, in the early 21st century, this model, due to political and economic changes in the federal government, state governments, foundations, and other historical financial supporters of university-based granted research programs, academic (generally university-based) research centers have been less able to adequately cover the full costs of performing such research. Increasingly it has been left to the research entity—in this case, a college, university, teaching hospital, or other research entity—to absorb and transfer such costs (5,6). This phenomenon is most apparent in the area of research-related “indirect” costs, known in federal jargon as “F&A” (facilities and administrative), as described in the recent article by Holbrook and Sanberg (7).

In this era of governmental attempts at austerity, federally funded research programs, such as the NIH, have suffered from repetitive “across-the-board” cutbacks. Thus, there are currently fewer total grant dollars available (9), and even well-entrenched, long-term NIH (and other similar) researchers and research-oriented institutions are finding it more and more difficult to maintain their same level of granted funding through these systems. For those researchers and institutions attempting to obtain their first “R01” or equivalent, the road is now profoundly difficult! There are no signs or suggestion that this situation will significantly improve in the
near future; in fact, the opposite has been postulated by many political and economic pundits (5,6).

In the arena of clinical patient care-related research, one of the evolving alternative methods of research funding is through industry-sponsored, “pay-for-performance” clinical trials. Industry-sponsored research platforms have “been around” for as long as industry has been bringing forth new products for the marketplace. However, there has long been an attitude of concern in academic, government, and other research circles related to the potential for financial abuse and the potential for false or misleading medical research information to be released through inappropriately or inadequately designed industry-sponsored clinical trials, which end up inappropriately benefiting the trial sponsor and the products they are trying to “bring to market.” Historically, these concerns have not been without merit. This has led to an attitude of disdain concerning industry-sponsored, pay-for-performance trials by many “academic” investigators and university centers.

In response to these concerns, over the past 10–15 years, multiple mechanisms of scrutiny, supervision, control, and systems designed on federal as well as industry levels, to remove the sponsoring (funding) company from the ability to control or effect clinical trial activities and outcomes upon their own products, have been instituted. These mechanisms include the following: the evolution of contract research organizations (CROs) and other similar organizations that now perform the majority of multicenter clinical trials management in the US and can contribute to the removal of direct contact by, and influence from, industry sponsors upon clinical trial sites and their outcomes. The appearance and standardization of national centralized institutional review boards (IRBs) can contribute to the monitoring of safety and ethical issues concerning clinical trials uniformly across multicenter trial sites. Federal acts have been created, such as the US Food and Drug Administration Amendment Act, section 801 (FDAAA 801, which requires that the elements of all interventional clinical trials be fully disclosed in national databases, such as clinicaltrials.gov), and the Physicians Sunshine Act as part of the Patient Protection and Affordable Care Act of 2010, requiring pharmaceutical companies and device manufacturers to report data about all payments and gifts made to physicians and teaching hospitals, to be disclosed on national websites such as the CMS website (2). The Omnibus Budget Reconciliation Act enacted by Congress in 1989, which includes a provision now known as the “Stark” laws, provides national transparency and oversight of industry-sponsored clinical research efforts (10). The federal Stark laws, among other provisions, govern inappropriate payments and “kickbacks” from industry-sponsored organizations to physicians performing clinical research. Other monitoring efforts include scrutiny by public sector entities, such as Pro Publica’s “Dollars for Docs” program (http://projects.propublica.org/docdollars/) that since 2009 has reported on payments to physicians, other medical providers, and healthcare institutions by major pharmaceutical companies (2).

There still always remains the specter of attempts at fraud or deception (6), but the same specter has also held equally true for more academically “acceptable” trial pathways, such as NIH-granted trials (1,3,4,8,11), whose activities are not subject to scrutiny by many of the above-mentioned laws and mechanisms. It is therefore incumbent upon each facility and their trials team to fully understand all laws and regulations governing clinical research and patient protection and to actively participate in the close and continuous supervision and monitoring of all research efforts, both “granted” and industry-sponsored, to best ensure adherence to all ethical, patient safety, and management standards and guidelines.

In this era of increasing difficulty in the securing of classical NIH and other similar “grants,” the “pay-for-performance” clinical trial pathway has some attractive merits for both researchers and the hospitals wherein the research is conducted. This option should be carefully evaluated by those centers wishing to start up or continue their funded research efforts and to create or maintain their research infrastructure. Increasingly, this pathway is a viable way for new research sites to financially “break into” the research arena and generate the revenues necessary to build the initial infrastructure needed to move forward with their clinical research efforts. Additionally, this pathway offers hospitals that have no direct ties to academic centers the chance to enter the clinical research market with the potential for additional revenue service lines for the hospitals so involved.

There are some significant differences in the “university” model of academic research funded
by granting mechanisms and “pay-for-performance,” industry-sponsored clinical trials. Many of the differences are too lengthy to discuss here but include differences in protocol and site budget development and acquisition, role of and compensation for clinical physician investigators who do not have protected time and are generally tasked to 100% clinical activities in an RVU-based environment, makeup of and funding for the site research teams, differences in availabilities of administrative funding for trial support, and mechanisms for research infrastructure development, to name a few. It is important to note that, as pay-for-performance clinical trials focus on in-hospital and/or clinic-outpatient patient populations and as industry-sponsored trials do not require research project “idea people” and proposal-writing or grant-writing teams (the protocols have already been developed and financial costs computed), they can be an excellent entry point into clinical research by potential investigators and clinical sites, such as nonacademic hospitals, that may not have or cannot afford large research infrastructures. They also can be a platform to encourage the development of potential clinical physician-scientist investigators, a group that a former director of the NIH classed as an “endangered species” (9). In the currently evolving clinical practice environment, this group of potential clinician investigators increasingly and paradoxically may have little or no previous clinical research experience, have no “protected time,” and find themselves employed in a 100% clinical RVU-based, practice-driven situation (progressively becoming the norm in the majority of hospitals and clinics) to enter into the arena of clinical research. As the “pay-for-performance” trial system fits nicely into the schema of a clinical facility’s RVU-driven clinical practice environment, these new potential clinician investigators may find that their facilities now encourage their participation in clinical trial activities (a “win–win” situation) rather than discourage such activities, as they have in the past. The lack of “academic” infrastructure requirements within the “pay-for-performance” pathway also means that there is a significant reduction in the large “overhead” costs that such “academic” systems generate, thus making pay-for-performance clinical trials attractive as an entry point for clinical research startup sites and for hospital and clinic facilities wanting to add an additional service-line revenue stream to their operations. Additionally, the pay-for-performance trial handles financial compensation exactly as described (pay for performance), and the majority of financial payments to the performing hospital, clinic, or other entity are made on a “per-subject-enrolled” basis with a billing and invoice system that is familiar to clinical, patient care facilities. This removes an additional overhead cost of having to support separate financial systems and personnel to track and manage granted trials, such as seen in university “grant offices.”

Thus, hospitals and other clinical facilities can utilize such “pay-for-performance” clinical trial opportunities as an entry point into the clinical trials arena. As these sites execute such trials and are able to build up their residual revenues from trial performance, they will be able to generate and expand their clinical trial team infrastructure. As they develop a cadre of seasoned trial team members and as their physician investigators become more productive clinical researchers, the facility can choose how to proceed. Some hospitals and facilities may choose to use their now expanded research infrastructure and trial residual funds along with clinical physician investigators who now have developed some clinical trial experience to start to develop investigator-initiated trial proposals and compete for NIH and other “granted” trial opportunities. Some facilities may choose to maintain their team and infrastructure as a revenue-generating service line for their facility. Many facilities may find that both pathways are now open to them. This trial pathway can also serve as a first step in recruiting new potential physician-investigators into the field of clinical research, thus expanding the existing pool of physician-researchers and encouraging RVU-based clinicians to involve themselves in clinical trials participation. In all cases, hospitals and other patient care facilities may find that the arena of clinical trial performance is a potential attractive addition to the services that they offer for their patients, and the availability of an industry-sponsored, protocol-driven, pay-for-performance clinical trials platform can be a relatively easy startup pathway for entry into the clinical research environment.

In summary, the changes in national and international financial conditions and the recent and significant economic downturn in this country have created a decrease in funding for the classical “university” academic model of research in the US. This situation, paired with the changing landscape of US healthcare and changes in the employment patterns and work
environment of potential physician-investigators has, in actuality, created a situation in which industry-sponsored, pay-for-performance clinical trials may offer some unique advantages over the classical “university-academic” model, especially to potential new clinician-investigators and to sites that want to start performing clinical trials without the benefit of a large “classical” research infrastructure. The current situation also allows clinical practice sites, such as nonacademic hospitals, clinics, and other patient care venues, previously not able to participate in the classic “university” model of research, the chance to enter the clinical research arena.

REFERENCES