or years, the pharmaceutical industry has recognized the inefficiencies of the clinical trial process. Paperless processes, standards, and real-time acquisition and access to data have long been the “Holy Grail” of the industry. The explosion of information technology has created tremendous possibilities for streamlining the clinical development process. For the first time in history, the industry can realistically expect to make a quantum leap in efficiency, capacity, and productivity. But several major stumbling blocks prevent substantive progress toward realizing the e-clinical vision on the horizon.

The lack of comprehensive standards (and supporting systems) that allow for free and easy exchange of data impedes the rapid and efficient movement of data between the sponsors, investigators, laboratories, and contract research organizations (CROs). This slows the process of execution and decision-making for any clinical trial. No integrated systems exist, nor any comprehensive system that can support the entire clinical trial process. Clinical trials are currently supported by clinical trial management systems (CTMS), data management (DM) systems, serious adverse events (SAEs) systems, and a wide variety of data access and reporting tools. Some are off-the-shelf packages, others “homegrown” solutions. In addition, individual companies may have complementary systems that are linked in unique or proprietary ways to support or to automate other aspects of their business (investigator payments, for example).

It is an enormous task to create an integrated, electronic solution that provides full support for even the fundamental pieces of a clinical trial: trial management and data management. To create such a solution, a single company—pharmaceutical, technology, consulting, or CRO—has to make a large investment in time and resources. A handful of the largest organizations can manage that alone, but a collaborative approach provides many advantages in terms of costs, speed of global development, and broad acceptance. The difficulty is to get what has long been a very conservative industry to take part in open discussions of these matters and to investigate an industry approach. Our purpose here is to share what Eli Lilly and Company
is doing in the e-clinical arena and to offer concrete suggestions that could serve as a model to help the industry move toward practical e-clinical solutions.

**The industry—progress and problems**

We have observed a number of difficulties for each element of the clinical trial industry that has tried or is trying to develop an integrated, comprehensive e-clinical solution.

**Pharmaceutical companies.** The task is probably beyond the financial means, or more likely the financial will, of all but the largest global pharmaceutical companies. In the past, large investments by major pharmaceutical companies to develop in-house solutions, even for data management alone, have seldom fulfilled their original promise. Furthermore, even those companies that have the financial capability and the institutional will to develop an integrated internal solution would risk

- failing to keep pace with technology.
- getting out of touch with the emergence of industry standards.
- waiting years for full implementation to realize benefits.

Despite the risks, some large pharmaceutical companies pursue e-clinical developments independently rather than waiting for integrated solutions to emerge in the marketplace. Licensing off-the-shelf tools and solutions, rather than customizing software solutions, can mitigate some of the risks noted.

Companies that embark on such an endeavor undoubtedly will need the assistance of selected technology partners and/or consulting firms. In fact, this model has been used for the past two decades and has led to modest, stepwise improvements in the application of technology to clinical trials. But such a model—whereby each company creates its own collaboration with technology and consulting partners—involves immense cost to the industry. With this approach, each company duplicates the efforts of others—developing standards and building interfaces between common off-the-shelf software products, for example. A collaborative group of pharmaceutical companies could eliminate duplicated efforts and reduce the cost and the risks for all.

**Technology companies.** Any single technology company would be stretched immensely to supply an integrated hardware and software solution today—or in the foreseeable future. Furthermore, technology companies do not have the content expertise to create a solution that matches the needs and requirements of the industry. A technology company embarking on this endeavor would be taking serious risks of investing resources and failing to meet the market need—or providing a set of tools that miss what is likely to be a moving target in clinical development.

**Consulting companies** cannot afford the up-front investment needed to create a solution. With business models based on fee-for-service and profit margins heavily reliant on billable hours, it is improbable that such companies can do the work required to build a solution without external funding and support. Nevertheless, consulting companies have been retained by pharmaceutical companies for individual, homegrown projects related to developing or implementing clinical systems that address a piece of the clinical trial process. The business model of CROs is also based on fee-for-service. Although some major CROs have tried to break out of the cycle of fee-for-service work by creating novel or advanced services that would command a premium price from the pharmaceutical industry, there are no clear examples of this business strategy coming to fruition in an integrated way.

**A collaboration model**

So where is the industry to turn to create an environment with effective, integrated tools to support clinical trial activities and thereby the clinical development process? Clearly the problem suggests the collaboration of some combination of the major players—pharmaceutical companies, technology companies, and consulting/service companies. How such collaboration is achieved—as working groups, a consortium, a not-for-profit corporation, a joint venture, or any other imaginable business construct—has been the topic of many discussions in private conversations and small forums involving selected constituencies. We prefer to call the collaboration a club to avoid any appearance of a preconceived notion of the business model. Finally, we note that the club is neither exclusive nor restrictive, but would be an open forum for membership.

Eli Lilly and Company has had internal discussions on this topic for nearly two years and has participated in a large number of such discussions with various constituent groups mentioned above. Because any information technology solution that merely enables clinical trial processes will be readily replicated or improved with the rapid acceleration of technology, Lilly believes that many aspects of any e-clinical solution are not a sustainable competitive advantage. As such, Lilly prefers to support broad, open, standard solutions that will benefit clinical development across the industry. Lilly sees these activities as noncompetitive, so we are committed to open collaboration to create a valuable and widely accepted industry approach to enabling clinical trial processes. This will also allow the cost of such solutions to be shared more broadly across the industry, to the benefit of each company involved.

At Eli Lilly, we have started down a path of redesigning our processes, standards, and systems in order to make some progress in this area in the absence of a club. We believe, however, that greater success can be achieved by working collabo-

![Figure 1](image-url)

Figure 1. Spheres of activity—the nesting of various electronic initiatives—that serve as a reference for the Lilly strategy for evolving e-clinical capabilities.
The essential kernel of the whole clinical development process, but those claims usually express hypothetical solutions or mere concepts. It does not take a long look at this picture to understand that creating a solution for any piece of this business—let alone an integrated solution—is a daunting task. We at Eli Lilly believe, however, that integration is a key to the acceptance and adoption of any future solution.

**The e-clinical realm**

The entire world is moving toward more electronic tools and processes. Many pharmaceutical companies have created business units or functional organizations that focus on driving toward a future state based on electronic solutions. Although much of this started with a commercial focus, electronic business concepts and processes have filtered their way into R&D organizations and even into specific divisions (e-clinical), specific functions (e-data management—eDM), and even specific processes (electronic data capture—EDC). Figure 1 depicts the nesting of various electronic initiatives and will serve as a reference for the Lilly strategy for evolving e-clinical capabilities.

An individual clinical trial in an e-clinical environment involves numerous distinct, but interrelated, activities. For this discussion, we can segregate these activities into those occurring during three segments of a study—start-up, conduct, and completion. Figure 2 depicts an integrated picture of these activities and their relative places on the timeline of a clinical study. We have identified major activities in the clinical trial process, but recognize that others may categorize or organize them in different ways.

**Integration of activities.** Each activity or small set of activities is the focus of software development by one or more technology companies. Many established and emerging companies are developing solutions to pieces of the clinical process based on their expertise, past history, or perception of an industry need. Some companies may claim to be working on end-to-end solutions to support the entire clinical trial or even the whole clinical development process, but those claims usually express hypothetical solutions or mere concepts. It does not take a long look at this picture to understand that creating a solution for any piece of this business—let alone an integrated solution—is a daunting task. We at Eli Lilly believe, however, that integration is a key to the acceptance and adoption of any future solution.

**Data is central.** The essential kernel of the whole clinical development process is the data. This is not a novel concept, but it needs to be stated explicitly because it drives all aspects of what we plan to achieve. Undoubtedly, one of the most valuable assets of a pharmaceutical company is its clinical data, which serves as the basis for submission, approval, labeling, and marketing of a compound. Useful drugs to meet unmet medical needs are essential to the viability of a pharmaceutical company. Without good clinical data—well organized, easily accessible, thoroughly documented data from well-designed trials—the value of a drug may not be fully realized. Efficient processes supported by well-designed systems will facilitate clinical development, but the data is the ultimate product of clinical development work. Thus, without a data-centric approach to developing any e-clinical solution, we are unlikely to be fully successful. The data is the foundation on which we build our entire effort.

For a solution to be effective, a common data structure or repository must be in place to facilitate the sharing of data and information. Without a single, syndicated data source, the enterprise will be unable to reach its full potential, because information emanating from even the best integrated system will be subject to question. Our primary focus, therefore, is on building a common data model and implementing data standards as the linchpin of a clinical data warehouse (CDW) that can be used across trials, across compounds, across therapeutic areas—indeed across companies and regulatory agencies as needed.

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**Figure 2.** The integrated picture of study start-up, conduct, and completion and the relative places of these activities on the timeline of a clinical study.
The central piece of the schema is aggregation. It is another aspect of the 3A model—access for analysis. Aggregation is crucial to driving down costs and waste in the clinical data management process. Acquisition of clinical data can be described as emanating from four fundamental sources:

- Subject-investigator interaction at a clinic, office, or hospital
- Labs, which include not only traditional clinical labs but also other diagnostic or bioanalytical tests
- Directly from subjects—a burgeoning area given the rapid development of personal technology devices to capture subjective (for example, symptoms) and objective (for example, blood glucose) data
- Partners in the clinical development process, which may include joint ventures with other pharmaceutical/biotechnology companies or traditional outsourcing to CROs.

An enormous number of new EDC companies are addressing the direct capture of subject data. Biotechnology companies and CROs form partnerships, and specialty labs emerge with new diagnostic and analytical technology for biomarkers. Presumably, the market will produce some sort of shakeout of the number of competitors in each of these arenas. But new technologies spawning new software systems and new diagnostic tools/labs will create an ongoing need to address numerous interfaces for pharmaceutical companies as they conduct any individual trial. Thus, robust data interchange standards are a necessary part of any future e-clinical environment.

Access. The last element of the 3A model is access for analysis and decision making. As our thinking has matured, we are realizing that access and analysis are two distinct, but related, concepts. Access is more about the casual or simple uses of the data to manage a trial or series of trials. It also allows assessment of processes for efficiency and productivity. Analysis is related to the inferential analysis (formal or exploratory) typically done by statisticians. The latter category of analysis requires additional
levels of documentation, because it is the basis for scientific conclusions about a trial and ultimately drug approval and marketing. For both access and analysis, we envision an environment that allows point-and-click generation of standard reports (for example, enrollment of subjects in the trial or adverse event reports) and the facility for ad hoc reporting that arises from unique aspects or issues in an individual clinical trial.

Our philosophy is to buy off-the-shelf tools as much as possible to build the 3A model at Lilly. As stated earlier, currently, no one tool can do it all—by definition, some level of system integration is necessary. Additionally, although we can buy some tools that are already industry standards (Oracle, SAS, and Microsoft Office, for example), it is not yet possible to buy a clinical data warehouse off-the-shelf. It is this integration and implementation of standard tools, and the implementation of newer tools, that are the basis of our interest in a club. For example, if one pharmaceutical company needs an interface between an EDC company and a central clinical laboratory, many other companies probably have the same need or could benefit from such an interface.

In our current industry environment, each pharmaceutical company might develop a slightly different approach to create such an interface. Or a pharmaceutical company might ask the EDC and clinical laboratory companies to adapt their systems to serve such an interface. Terms such as Oracle tables and SAS datasets convey immediate meaning to the various parties involved.

Although uncommon in the pharmaceutical world, and even more uncommon in R&D and clinical development, business models have emerged around this layer of the pyramid over the past few years. At this level, outsourced services may be bundled with the hosting layer and be contracted with an application service provider (ASP). The term is widely used, even though this model is a phenomenon only recently enabled by the Internet and the technology explosion in telecommunications and networking. Because of its novelty, and because ASPs are generally in their infancy, the term is often misunderstood. It can be used to describe a variety of different IT outsourcing business models.

Application software layer. The next layer is the common application software layer. This includes software that is used by many, but which may have only a minority share of its market space. Examples include Oracle Clinical for data management, PhaseForward’s InForm for Web-based data management, IMPACT for clinical trial management, Documentum for document management, Clintrace for serious/spontaneous adverse event management, and Spotfire for data exploration/visualization. This is where a club model could come into being as a business construct. A group of companies could collaborate on the selection of a primary software tool in each of these business process areas (that is, data management, clinical trial management, adverse event management) and jointly fund the integration of these tools to create an e-clinical platform for the execution of clinical trials.

Furthermore, the collaborators could agree on the infrastructure layer and a suitable hosting service provider. They could negotiate hardware and software integration with the selected

Collaboration concepts
We depict the integration of hardware and software as a hierarchy, with layers that range from highly standardized to unique (Figure 4). The most standardized layers have the broadest applicability and largest potential user base, while the unique layer has a narrow focus and specialized user base. Therefore, we represent it as a pyramid.

The hardware layer at the base of the pyramid consists of the computer system hardware, networks, operating system software, data storage, and the physical environment to house that equipment. This layer—commonly referred to as infrastructure—might also contain some software related to data interchange. For example, as the industry gains momentum for industry standards around electronic data interchange through Extensible Mark-up Language (XML) technology, one can imagine including such definitions and the software needed to manage data interchange as part of this layer.

Business models around this layer are well defined and have been in existence for the past two decades as companies' need for IT (information technology) increased dramatically. Outsourcing at this level might be arranged with a hosting service provider, an application infrastructure provider, or a management services provider.

Standard application software, the next layer, is considered standard not because some standards body or regulatory guideline endorses it, but rather because it has gained a level of ubiquity in the clinical drug development business. Examples include Oracle software for database creation and storage and SAS software for statistical analysis. Such software allows for easy communication between people who manage data and those who analyze it. Terms such as Oracle tables and SAS datasets convey immediate meaning to the various parties involved.

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vendors whereby each party (pharmaceutical companies and software and hardware vendors) contributes real and intellectual capital. Obviously, to share ideas openly, pharmaceutical companies in the club would have to have similar philosophies about what is competitive and noncompetitive regarding clinical trial logistics and execution. In that way, the club would become an application service provider, and the standard software layer would be expanded to meet the needs of the pharmaceutical club members.

**Unique software applications.** The top layer represents software applications that are unique to a particular pharmaceutical company, for example, an interactive voice response system (IVRS) or an investigator payment system. Those applications considered noncompetitive by any pharmaceutical club member could be offered to the club as intellectual capital and incorporated into the standard software layer if other club members found them useful. Alternatively, if the club was unwilling to incorporate such applications into the ASP, the individual company could embark on its own separate proprietary integration effort. The scope of any such integration could be much smaller and less expensive because the club would share the cost of other system integration.

Finally, the implementation of the club as application service provider within a company would be at the discretion of each pharmaceutical club member. Training, organizational change management, and migration plans to the new, integrated systems could all be done internally or with each company’s desired consulting/business integration firm. Each club member could take as little or as much risk as desired in terms of the speed and scope of its company’s implementation.

**A challenge to the industry**

We have argued that creating a comprehensive e-clinical environment is an enormous task, because it involves the integration of many disparate pieces of software to manage the many facets of clinical trial execution. It is very difficult for any one company to create such an e-clinical platform in any reasonable period of time. Furthermore, we contend that certain aspects of clinical drug development should be considered noncompetitive for the pharmaceutical industry—for example, data standards, choice of hardware, and the choice of certain software. Few, if any, CEOs of pharmaceutical companies consider their company’s stock price tightly linked to the way the company collects data, the software it uses to manage adverse event reporting, or the hardware it uses to store clinical data. What is most likely of interest to CEOs is how to reduce costs related to those transactional activities and how to increase speed and efficiency.

We have proposed a business model for developing an e-clinical platform with mutual benefit to all parties involved—pharmaceutical companies, technology companies, and business consulting/implementation companies. The model is based on a strategic choice to develop an integrated suite of best-of-breed tools rather than developing a single suite of integrated tools. We have described how a collaboration—a club—could be developed by considering various layers of standardization of hardware and software. We have proposed a way to start small, using a 3A model for handling clinical trial data. And, we contend that a club could expand capabilities more rapidly and less expensively than any one company could do alone.

Finally, because Eli Lilly and Company views many of these areas of data management and clinical trial management as non-competitive, we enthusiastically support CDISC and its collaboration with HL7. Furthermore, we are interested in communicating with others in the pharmaceutical industry who have like-minded goals about developing open collaboration around an e-clinical platform. In that regard, we are aware that CDISC is developing an interactive portion of its Web site where companies can post their data standards, SOPs, and other information that will accelerate the development and implementation of standards across the industry. Eli Lilly and Company plans to be very open with posting/publishing its standards and are also enthusiastic about what others may contribute.

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