



THE NEW FACE
OF CLINICAL DATA MANAGEMENT

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» By Andrew Schafer, Senior Director, Strategic Resourcing, Quintiles Global Data Management & Biostatistics

In today's biopharmaceutical industry, the rapid collection of high quality clinical trial data isn't dependent on technology or software applications, nor is it dependent on process or process reengineering, nor is it dependent on financial business models. Rather, it is dependent on people.

Ultimately, people are responsible for turning data into meaningful information, which is what the biopharmaceutical industry needs to be successful. We need information to create better compounds, to design better protocols and to make faster go/no-go/alter assessments on compounds in development.

What the biopharmaceutical industry does not lack is data. With very little effort, one is able to quantify how many prescriptions have been filled for a particular drug, or how many oncology products are in Phase III, or what the average query rate is for cardiovascular compounds in Phase II. This is nothing new, so what has changed that makes people so important?

LIFE BEYOND TRADITIONAL DATA MANAGEMENT

Electronic Medical Records

Increasingly, the industry is turning its attention to the use of electronic medical records (EMRs) for clinical development purposes. The use of this technology, and the data held within these systems, is a prime example of how clinical data management is morphing from straight data collection into being an information provider.

» Spending on EMR applications globally will increase more than 20% annually through 2012*. This rapid growth will foster both differentiated service offerings and consolidation and it is these two forces that will act together to drive the widespread use of EMR data/applications in clinical trials.

* Source: Opportunities in the Electronic Health Record Market, Datamonitor, December 2007

The data held within EMRs can help clinical development in a number of ways, but the path to value will not be short or easily traveled and will require investments in capital, human resources and time. Protocol writers can use EMRs to perform feasibility analysis; biostatisticians can use them to do scenario planning; and clinical operations can use EMRs to find clinical investigators and patients. Ultimately, it will be up to the data managers to manage, access and control the data that has so many potential benefits across an entire clinical development program.

Adaptive Clinical Trials

The increase in the sheer volume of data is one challenge facing data managers; another is the speed at which quality data is collected. As adaptive clinical trials become more commonplace, speed of data collection becomes the driving force of value. For adaptive designs to truly provide value, data needs to be collected quickly and delivered into the hands of the statisticians for analysis and decision-making.

The effects these changes in data analysis strategy have on the traditional data management organization are twofold: (1) SOPs and training will be needed to work in this new environment (e.g., when is data clean enough for analysis?); and (2) a much closer working relationship will be needed between data management and the biostatistics and clinical monitoring organizations.

In a trial designed with adaptive qualities, data cannot be batch processed; individual attention must be paid to each investigator site, each patient and each data field. Adaptive designs do not lend themselves to a heads-down approach to data management. Rather it puts a premium on data managers who excel in a fluid environment, pay great attention to detail and have the ability to successfully communicate outside of their organization by leveraging their working knowledge of clinical and statistical operations.

HISTORICAL CONCLUSION AND IMPLICATIONS

It is no secret that the biopharmaceutical industry is in a state of constant flux. New product introductions are down, but early-stage pipelines are strong. Biopharmaceutical stock prices are down, while service provider stock prices are higher. Financial pressures are mounting, lay-offs are commonplace and adding staff at some companies is nearly impossible. Patents are expiring, and mergers, divestitures, in-licensing and out-licensing deals are happening every day. From a business perspective in

the world of clinical data management, a lot of the low-hanging fruit has been, or is in the process of being, picked. Outsourcing clinical data management functions to low-cost regions to take advantage of labor-arbitrage conditions is no longer a differentiator. Process reengineering efforts help to further drive economic benefits, but clinical development is not assembly-line manufacturing, and any reengineered process also requires flexibility.

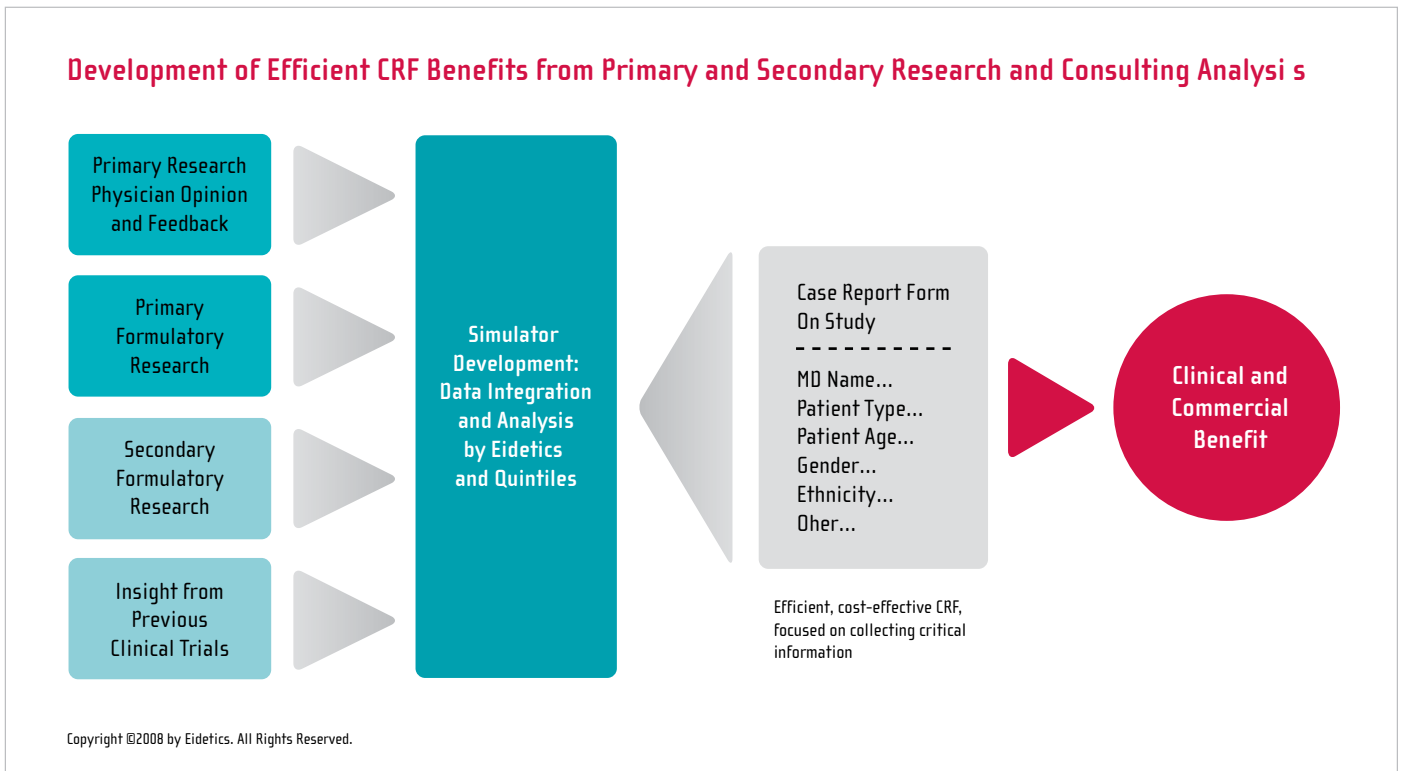
In the legacy world of clinical data management, there are certainly a few routine processes that can be made more efficient and some of these processes can even be accomplished in isolation from the rest of the clinical development organization. However, as financial pressures on biopharmaceutical companies continue to mount and heads of R&D look to extract the most value possible from their assets, they are examining the entire development cycle to increase efficiency while maintaining the highest level of patient safety. To maximize asset value, data must be turned into information and used before, during and after a clinical trial. A strategic approach to the design, collection, manipulation and analysis of data across the clinical development organization is a necessary step to maximize the value of the asset. That said, an outsourced functional service provider approach can work and provide great value to a biopharmaceutical company. However, the partnership between the biopharmaceutical company and the service provider has to be led on the service provider side by people who understand the entire clinical development spectrum and how data fit. It is this knowledge and integration that provides tangible long-term value and places a premium on having access to the right people with the right skill set when needed.

Heads of data management departments should use this time as an opportunity to reposition their organization. They should use information to add value to the broader R&D initiatives as today's strong early stage pipeline works its way through the development cycle. One way to get started might be to leverage your development partners. Biopharmaceutical companies that outsource some or all of their clinical data management should leverage the data that their service provider partner should already have in its data warehouse. Service providers see a lot of different study designs; they see a myriad of SOPs and standards; they work with multiple systems and do this on a global basis across all therapeutic areas and phases of development.

Smart and experienced service providers combine their historical performance data with simulation and modeling techniques. When this

is overlaid with a deep understanding of the nuts and bolts of clinical development, it produces some very powerful, actionable information. This information is being used to design better protocols, conduct better feasibility assessments, set recruitment expectations, develop statistically meaningful metrics, better plan resource utilization, increase the chance of successfully developing an asset and serve as a basis for process redesign. Taking this holistic approach to information management will have a direct impact on the bottom line. Although obviously not mutually exclusive, a biopharmaceutical company can save more time and money on one well-designed protocol and by monitoring the performance metrics of a single trial than it can from replacing 50 data entry people in New Jersey with 50 people in Bangalore, India.

Apart from the economic benefits accrued by using information, rather than simply collecting data, the impact on patient safety should not be



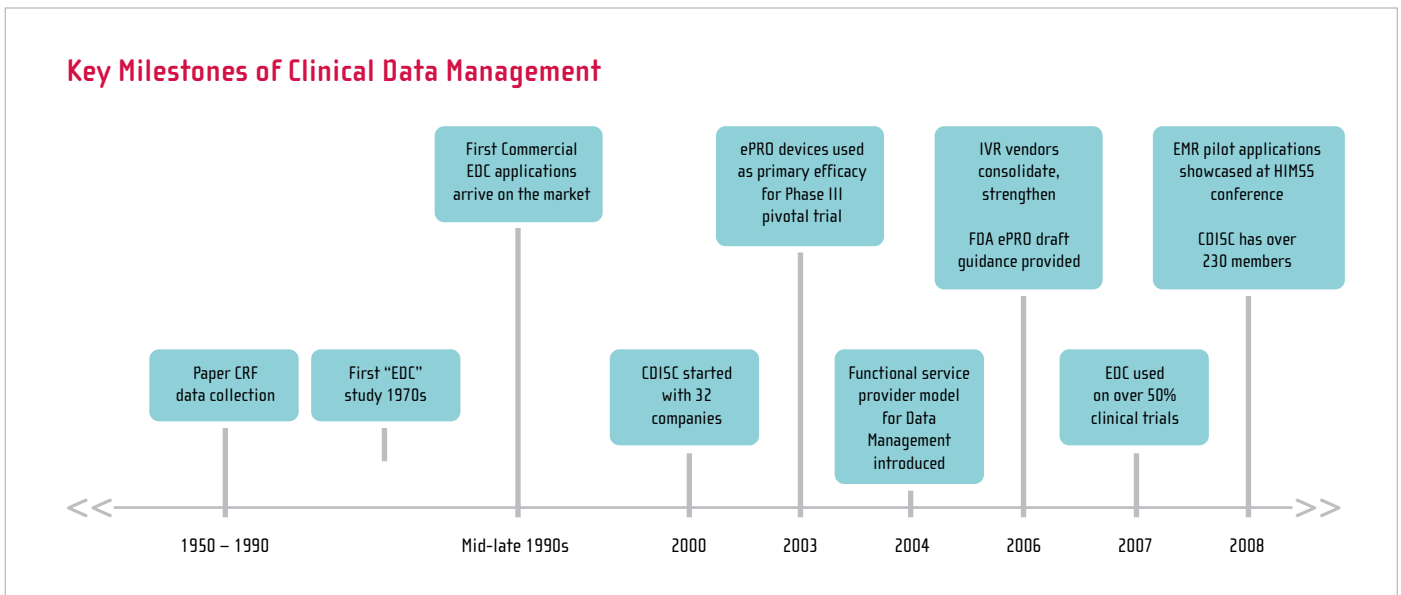
overlooked. By establishing processes for effectively using data and data standards across a clinical development organization, patient safety can be enhanced. For example, suppose recruitment is about to begin for a clinical trial. First, by looking at historical data from a variety of sources, a safety profile is established. Second, armed with the historical information, a plan anchored in predefined data standards is developed that integrates information from clinical operations, data management

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and biostatistics. Along with software tools, this will allow medical monitors visual access to an integrated dataset during the trial to make near real-time decisions regarding treatment regimens. In order to generate these benefits, it takes a commitment to standards, access to data, intelligence to interpret the data and subject-matter experts to work across the development organization.

Thinking beyond the traditional service offerings or job functions within a data management organization will be critical to providing value to the organization and its products in development. For example, using data and results from past trials and integrating those findings with programs designed to develop case report form (CRF) or electronic CRF (eCRF) content can provide significant value. Designing primary market research studies that test treatment alternatives in real-world settings and then translating those findings into CRF design is just one example that provides powerful clinical and commercial results. (See chart on pg 4.)

As previously discussed, the speed of change in clinical data management is accelerating. The changes to clinical data management in the past five years dwarf those of the previous 15.



Change is not easy, and it is certainly not easy in global organizations that employ hundreds or thousands of employees. Clinical data management organizations must embrace change and champion it throughout their organization.

Clinical data management is not about data. It is about people. It is about training people or finding people who understand that their role

in drug development lies well beyond the CRF—it lies with turning data into information. Data integration and standards will help. But in the end it will take knowledgeable people, equipped with the right tools, to successfully manage the new clinical information centers that will evolve from today’s clinical data management organizations.

CLINICAL DATA MANAGEMENT

Over the past ten years, a variety of forces have influenced clinical data management organizations.

ELECTRONIC DATA CAPTURE

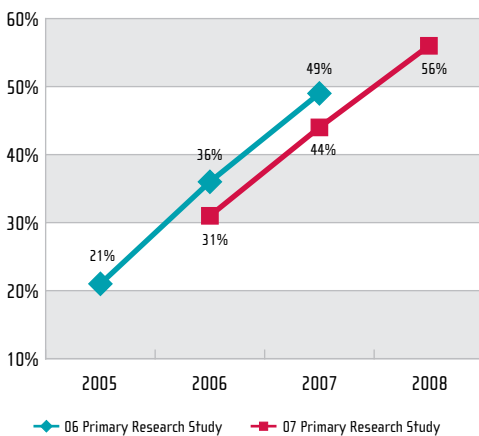
Today, Electronic Data Capture (EDC) is mainstream. There are a number of stable, mature providers of EDC applications and the vast majority of large biopharma companies and CROs have selected preferred EDC technology providers. The “beta testing” phase is complete and has evolved into full-scale implementation. However, getting to this phase has been a long road, and roughly half of all clinical studies running today are still paper-based.

The road to EDC adoption has been fraught with many potholes and U-turns along the way. An early, simplistic view of EDC was that it simply digitized the traditional paper case report form (CRF), thus most organizations made their data management departments accountable for EDC implementation. The early implication of this decision was that data management implemented EDC, but no other stakeholders in the clinical development organization changed their processes. As a result, the promises of EDC did not rapidly materialize. Through trial and error, and in some cases a lot of consulting time, the industry determined that EDC is, in fact, a clinical tool.

With that realization, data management organizations were saddled with three, rather large, imperatives: (1) evaluate and select an EDC technology partner that gives the organization the functionality it needs at the best price; (2) re-train your data managers, programmers, coders and validation staff to be able to work on EDC and paper studies; and (3) be the change agent for the company and lead the introduction of EDC into the broader clinical organization. All of this stretched the roles and responsibilities of traditional data managers.

EDC Adoption

2006 vs. 2007 Study Comparison of EDC (% of studies)



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DATA SOURCES

As the drug development industry matured and became financially successful, the industry faced the same forces other industries have faced, such as rapid specialization. Successful industries breed not only competitors, but also complementary businesses that serve as specialists to the broader industry. To a large extent, this phenomenon, along with advances in IT infrastructure and applications (software and hardware), have led to an explosion in the number of disparate data sources that combine to form the final data set for analysis and regulatory submission.

Just sit back and think of the potential sources of data that could be associated with a single trial, not to mention a complete clinical program. For example, within a clinical program, data could be collected on paper CRFs and via an EDC application (eCRF); could include either paper diaries and/or electronic patient reported outcomes (ePRO); could include both central lab data for esoteric testing and local lab data for safety testing; could use IVR data for randomization and/or clinical supply management; could have ECG data; and, to boot, the safety data could be held in a separate database. That's a lot of data coming from a lot of sources at different times—with different levels of cleanliness, in different data formats and with different SOPs for cleaning and reconciling the data into one clean database.

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STANDARDS

The CDISC era is well upon us and the benefits have the potential to greatly enhance the process of clinical development. However, the formulation, introduction and adoption of data standards will, in the short run, add to the growing number of diverse areas of expertise required to be a successful data manager. No longer will studies be looked at in isolation and because CDISC cannot possibly cover every data element captured in a clinical trial, biopharmaceutical companies are left filling in the blanks. After a company creates its own CDISC standard, libraries have to be developed, processes and SOPs reviewed and updated, staff trained, specification documents created for outside vendors and data repositories created, mapped and transformed. Today, clinical development organizations are expecting to use data from past and ongoing studies to make informed decisions about current and future products in development. On a daily basis, data

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» Quintiles Transnational Corp.
Post Office Box 13979
Research Triangle Park, NC 27709
+1.919.998.2000
www.quintiles.com

managers receive calls from people and places in their organization they have rarely interacted with before.

ALTERNATIVE DELIVERY MODELS

Combine all of the new initiatives now facing a data management department (EDC, standards, exploding data sources, etc.) and then consider that the majority of large pharmaceutical companies deem data management to be a non-core activity, thereby outsourcing many aspects of their data management activities to CROs and consulting companies. Now you begin to understand the complex world data managers live in.