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In the next issue of
EDC Today:

Vendors, Products, and
Suppliers: A Consumer's
Guide to the EDC
Marketplace – Part II

Vendors, Products, and Suppliers: A Consumer's Guide to the EDC Marketplace – Part I

Welcome to our ninth issue! EDC Today is an independent publication about current information and issues in Electronic Data Capture (EDC) strategies and technologies for the Biotechnology and Pharmaceutical (biopharma) industry. Each month we examine topic areas related to EDC theory, technology, practice, or implementation.

Feeling increasing pressure to conduct clinical trials more cost effectively, biopharmas are turning to EDC systems to help them produce cleaner data faster. At the same time, industry observers are predicting that the FDA will soon migrate entirely to electronic record systems and require sponsors to follow suit. These converging forces create an environment ripe for the widespread adoption of EDC strategies. Biopharmas hoping to implement EDC systems have a range of options – from contracting the entire process to external vendors to performing the entire process in-house. Choosing from these extremes and all the options in between requires a clear understanding of the various technologies and service providers available. In this issue, we introduce our analysis of the state of the current EDC marketplace.

Although the use and submission of electronic records are currently voluntary, many within the biopharma industry predict that ultimately the FDA will migrate entirely to requiring electronic record systems. Even now the FDA has an internal mandate to be able to accept fully electronic filings by June 2003.

While this looming deadline does not require industry sponsors to submit electronic filings, it certainly foreshadows an evolving preference for electronic data over paper records. Many companies want to be prepared for this possibility. Colin Spink of IBM offers a succinct summary of the impending shift to electronic record systems:

“The move towards electronic clinical trials is just a matter of time. With pharmaceutical companies increasingly submitting trial data electronically, it is

inevitable that the FDA will eventually demand all information be provided in this format — although no date has yet been set. With that in mind, and the proven business benefits that EDC can deliver, undoubtedly the successful pharmaceutical company of the next decade will have harnessed EDC across the majority of clinical trials.”¹

Concurrent with the growing allure of electronic data management, there has been an increase in pressure to perform clinical trials more efficiently. In their Drug Information Journal article about industry best practice metrics, Ron Fitzmartin and Kim Nitahara comment on the trend of increased industry pressure:

“Over the past decade, internal and external pressures on the biopharmaceutical industry have posed the challenge of decreasing the time and cost associated with product development, in particular, clinical trials process. While cost and time must decrease, quality must be maintained or improved. In an extremely competitive market, companies are constantly striving to expedite the drug development process by implementing more efficient and effective processes and systems.”²

Given these converging trends, some industry observers believe that EDC's time has come. In its report on electronic data capture, Forrester predicts that for industries responding to the increased demand for more clinical trials, Internet-based EDC applications will become indispensable and widespread:

“Use of Net-enabled EDC in new trials will show double-digit growth nearly every year through 2006...After a decade of false starts and failed expectations, electronic data capture for clinical trials is ready for broad adoption.”³

Though current use of EDC varies widely – among the top ten pharmaceutical companies, EDC use in clinical trials ranged from 0%-60% with a median use of 10%⁴ – most estimates point to a surge in EDC implementation.

About EDC Management:

EDC Management was founded to assist biopharma companies plan, prepare for and implement Electronic Data Capture (EDC) strategies according to their data management goals and objectives. We do not sell or endorse any specific EDC software application or vendor.

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Andrus and Carlson’s SCDM report states that 38% of survey respondents indicated plans to pilot or implement EDC within the next 12 months.⁵ According to the top ten pharmaceutical companies’ future plans, the median use of EDC will rise to 15% for 2002, 30% for 2003, and 53% for 2004.⁴

Though reasons behind the slow adoption rates of EDC systems are complex, it is clear that a lack of confidence in current EDC vendors is a significant concern. Many biopharma companies have decided to wait for the EDC vendor shakeout. According to Ron Waife, eight new vendors emerged in 2000, and of the existing vendors, half of them have had material improvements or declines in their financial status. “This must give sponsors pause,” Waife concludes.⁴

Currently there are over 60 EDC vendors, many of which produce products that aren’t highly evolved and have yet to become profitable. Though some vendors have attained a sophisticated level of development and produce quality products, the outlook for many EDC products is dubious. Biopharmas are often motivated to adopt new processes and products by a desire to improve their financial standing. Given the still emerging market, engaging in relationships with new vendors necessarily requires a certain amount of risk.

Given the state of today’s market, biopharmas can choose from one of three primary options for implementing EDC: contracting with Electronic Contract Research Organizations (eCROs), contracting with Application Service Providers (ASPs), or installing one or more products in-house. The risks and rewards associated with each option are presented below.

Options for Implementing EDC

eCROs

For biopharmas, eCROs offer a critical service: during the course of the clinical trial, they provide EDC systems for collecting and cleaning data and, at the conclusion of the trial, they deliver their products (e.g., SAS DataSets™).

The primary advantage of contracting with an eCRO is that eCROs absorb the risk of the EDC product. For example, because eCROs have responsibilities to deliver their products, they must manage and overcome any data capture or analysis problems that arise.

Conversely, there are several disadvantages of contracting with eCROs. First, working with an eCRO may be more expensive for biopharmas than performing the same duties in-house. In addition, using an eCRO may reduce the sponsor’s level of control over the trial. Sponsors may not receive interim information that could be useful in evading or curtailing data problems. Similarly, sponsors may become too detached from the day-to-day details of the study to make informed study-related decisions.

A number of companies provide eCRO services, including Target Health, Incorporated, PharmaNet and Datasential. Common eCRO services include: total trial services, trial management, site management (i.e., an eCRO may already have access to a number of sites already familiar with EDC

process), protocol development with EDC in mind, and preparation and submission of regulatory documents (i.e., New Drug Applications) to the FDA.

Other potential advantages of working with eCROs include:

- Unlike some sponsors, eCROs have extensive training in EDC
- The eCRO’s experience with EDC brings increased functionality, including more efficient eCRF’s, standard forms and checks, and more user friendly edit checks
- Responsibilities (and associated burdens) regarding site assessment and training are shifted from sponsors to eCROs
- Compared with other vendors, there’s greater stability due to contractual agreements to deliver EDC datasets to sponsors regardless of problems that may arise

ASPs

ASPs are companies that provide hardware, servers, networks and network management, software and software management, help desk, maintenance, and other services for fixed monthly or annual fees. In effect, ASPs are a way to outsource computer systems and infrastructure. For biopharmas, ASPs offer software and hosting services that enable clinical data collection and cleaning and produce SAS DataSets™.

In their book, *Building Corporate Portals Using XML*, Clive Finklestein and Peter Aiken predict the growing importance of ASPs:

“This is a radical move that will transform desktop computing as we know it. It will provide ubiquitous computing through the Internet and the intranet. And with a move to wider bandwidths on the Internet – with higher data rates available also through wireless computing via PDAs or mobile phones that access the Internet for email and browsing – we will soon be able to work not just from the office, but from anywhere. In a few short years these ASPs will become Information Utilities for the future.”⁷

Biopharma companies must consider certain issues when choosing the ASP option. On the plus side, ASP vendors absorb the risk of setting up the IT infrastructure and maintaining servers and server access. ASPs can also be constrained by service level agreements (SLAs) to deliver software, access, and SAS DataSets™ according to the sponsor’s specifications. Though ASP will have physical control of the data much as a CRO does, how the sponsor can access that data – whether the sponsor will have real-time access, for example – will be negotiated as part of the SLA. Sponsors will still need in-house IT talent to understand and monitor the remotely controlled database(s) and applications, even though the ASP provider may handle many of the details.

Among the disadvantages of working with an ASP, there is probably greater risk associated with ASPs than with eCROs since sponsors will be tied to an ASP vendor for the length of a clinical trial. Should the vendor fail, the

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sponsor will endure great pains (both logistical and financial) in transferring to another product. Another potential disadvantage is cost: using ASPs can be more expensive than managing the same responsibilities in-house. In addition, getting interim clinical trial information may be more complex and costly, and sponsors may not have as much control over the data as desired.

When considering the services provided by ASPs, it is important to remember that the responsibility for the integrity of the data lies ultimately with the sponsor. Hardware and software outsourced through an ASP must still be validated. Because the vendor who originally created them should have heavily tested the hardware and software, the sponsor should not have to repeat those tests. Instead, documentation of the design-level validation and testing should be available for auditing. However, sponsors do need to undertake and document functional level testing. This includes identifying and documenting the effects of any known limitations or problems relevant to the sponsor's study. Finally, validation requires a detailed audit of the ASP.

Today's biopharma market is rich with ASPs. DataTrak⁸, CB Technologies, Inc.⁹, and Etrials¹⁰ are three well-known ASPs. Advantages offered by ASPs center on data center (web server farm) hardware and software support.

Other potential advantages of working with an ASP include:

- Competent and highly trained IT infrastructure
- Web server hardware, scalability, load balancing
- Redundant components which insure product availability (i.e., EDC application will nearly always be "on-line")
- Help desk/technical support
- Web-based access to remote servers that run all study-related applications
- Ability to export data into several formats
- Automated back up of clinical trial data
- Protection from viruses that disrupt study applications on local machines
- A single portal (i.e., Webpage) through which users can access all the information they need to manage trials and communicate with fellow users
- Freedom from the risk of running out of hard drive space on local machines
- Freedom from having large applications installed on local computers
- Strategies for enrolling and randomizing patients
- Access to various levels of consulting, process change management, and customer support

Bringing Products In-house

The third option for sponsor companies involves bringing EDC products in-house. Sponsors choosing this option purchase both hardware (e.g., servers) and software that enable both the collection and cleaning of clinical data during the trial and the production of SAS DataSets™ at the trial's conclusion.

The primary advantage of this route is that the sponsor has complete control over the studies they run and more flexibility than they would have with an ASP or eCRO option. Sponsors bringing EDC systems in-house have the most flexibility and control over the trial set-up, the trial execution, and data collection and management. However, this flexibility comes at a high price – bringing EDC systems in-house entails the greatest amount of risk for sponsor companies. It requires the greatest commitment of internal resources whose responsibilities include system validation and training.

Several vendors offer products designed for sponsors who choose to bring EDC systems in-house. Two popular vendors and their products include Oracle's Remote Data Capture (RDC)¹¹ and eResearch Technology's eDataEntry (eDE).¹²

Other potential advantages of bringing an EDC product in-house include:

- Can use existing IT staff
- Can use existing help desk
- Has more control over resources
- Has more control over data
- Has more control over integrating in-house computer systems
- Better able to deliver competitive advantage
- Over long term, may be more cost effective (at least in terms of CRO profit margin savings)
- Integration of the EDC applications with the clinical data management systems (CDMSs)
- Ability for multiple users to access data
- Secure network access via a virtual private network (VPN) or password-protected dial-in capability
- Access to various levels of consulting, process change management, and customer support

EDC and Pre-Existing Legacy CDMS Solutions

Creating EDC datasets that are useful to sponsor companies should be the ultimate goal of any EDC vendor. Though EDC promises additional advantages, such as producing EDC datasets more quickly and cost effectively, there is no getting around the fixed end point: electronic files that meet FDA standards. At this time, EDC datasets intended for analysis and eventual submission to the FDA are presented in SAS. Soon they will most likely need to adhere to the Clinical Data Interchange Standards Coalition (CDISC) data model. Other electronic file standards, such as the use of PDF files, will most likely also need to be followed.

Traditional CDMSs produce records that eventually meet these requirements. Typically CDMS systems also manage additional data processing details, such as loading batch data, checking lab data against reference ranges, handling dictionary encoding, managing randomization and blind breaks, and performing complex edit checks.

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Careful consideration will be required to decide whether sending EDC datasets to an existing CDMS is (or will be) advantageous. EDC datasets stored in a CDMS may or may not be more easily secured, transformed, and combined than they can be in a SAS DataSet™ “database”.

If the eCRO provides SAS DataSets™, the sponsor might be in a position to move into the submission phase of conducting a study. Similarly, if the ASP provides SAS DataSets™, the sponsor might be able to move on to the submission. In either case, the sponsor might also need to provide lab data, coding data, or other data to the EDC vendor in order to complete the EDC datasets before receiving a “final” set of SAS DataSets™. Or the sponsor might need to complete the SAS DataSets™ received from the eCRO or ASP. If the sponsor performs the EDC study in-house, some of these issues might be resolved early on in a way that is advantageous to the sponsor (e.g., being able to retain and use a time-proven legacy AE autoencoding dictionary and methodology.)

Despite some possible advantages, retaining legacy CDMS systems present significant challenges to companies wishing to implement EDC. Regardless of the EDC solution used – laptop systems, web-based systems, handheld devices, or scan/fax-based systems – data collected in the front end will probably need to be loaded into the back-end CDMS system later. Therefore, any company using a separate EDC system might be forced to perform many tasks twice – once for the EDC system and once for the CDMS.

In a company white paper, Oracle describes the challenges and obstacles that might arise when both an EDC system and CDMS are employed:

“Definitions of the study CRFs and the corresponding data entry screens must be created in the CDMS and the EDC tool. Edit checks must often be written in both systems, patient and investigator lists must be redundantly defined, and careful cross-checking is needed to confirm that the two sets of definitions are consistent. Once the study commences, data must be fed from the investigative sites to the EDC system, then from the EDC system to the CDMS. Difficulties arise when the CDMS catches data problems that cannot be trapped by the EDC system. For instance, if the CDMS determines that a lab value from batch-loaded data is out of range, how should the investigator be notified that an adverse event page needs to be completed? If a discrepancy can somehow be generated and broadcast to the EDC system, how can anyone subsequently determine which system is in charge of the discrepancy? If an adverse event description is determined by a medical coder to be ambiguous or in need of splitting how is this (back office) request to be communicated to the investigator? These very real issues often require messy custom interfaces and/or manual intervention. If you add in the requirement for

validating the whole environment according to industry guidance and regulations such as 21 CFR Part 11, you often find that the total work required is greater than just doing the study using paper.”¹¹

The degree to which these issues will be problematic varies from sponsor to sponsor according to individual business practices. Still, when selecting among EDC solutions, these issues should be considered, and solutions should be chosen accordingly.

Conclusion

Some firms may be tempted to let the market mature before making the transition to EDC-facilitated clinical trials. However, the decision to wait means losing out on the benefits of EDC that other firms are already beginning to realize, including more effective management of clinical trials, faster time to market, and improved data quality. For example, a recent survey that compared EDC to the paper-based process in ten phase III studies found that the number of data queries per subject in the paper process was 5-20 times greater than with EDC.¹ The survey also found that the cost of raising and resolving a query with the paper process was six times greater than the cost of resolving queries with EDC.¹

The next several years are likely to bring a significant EDC market consolidation. Given the number of companies currently using multiple products depending on their clinical trial needs, it is safe to assume the EDC market will ultimately support 6 to 8 companies, which is about twice the number of existing pre-EDC CDMS products. Not many EDC products will survive the market shakedown, with a few emerging as a result of vendor consolidations. As an example of the consolidation trend, in a press release dated 10/15/2002, eTrials and Arracel have agreed to merge.¹⁴ More of these announcements will undoubtedly appear in the near future.

It will be difficult to know when the EDC market has truly settled. One possible measure could be when a particular solution outlasts the longest clinical trials. Another measure could be when one feels a product offering will be available in basically unchanged form for about 10 years. For biopharmas, these unknowns remain powerful reasons to avoid the expense, training, and commitment of internal resources until products are likely to persist for at least the life of a long-term study. In such a market, it may make the most sense to work with an eCRO or an ASP that can absorb some of the risk.

While the market remains unsettled, biopharmas need to assess the risk associated with new technology. Future market consolidation and the evolution of vendor shakeout will increase biopharma’s comfort level in selecting vendors, will provide fewer products for investigators to potentially learn, and will potentially propel the development of more refined products.



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- ⁵ Andrus, J., K. Carlson, et al. (2001). *Analysis of Current and Future Use of Technology*. *Data Basics: A Newsletter of the Society of Clinical Data Management* 7(3): 7-13. Jonathan Andrus of Teratec Development Corporation, Ken Carlson of Pfizer, and Tom Mahler of Phoenix Data Systems are members of the Society for Clinical Data Management (SCDM).
- ⁶ Target Health. *On Target*. October 20, 2002. Available at: <http://www.targethealth.com/10202002.htm>
- ⁷ Finklestein, Clive and Aiken, Peter. *XML and Corporate Portals*. White paper presented at the Information Resource Managers conference, October, 2002, Dallas.
- ⁸ DataTrak, Inc. www.datatraknet.com
- ⁹ CB Technologies, Inc. www.cbtech.com

Who's behind the research?

Our lead researcher, Kirk Mousley, PhD received BS and MS degrees in Electrical Engineering from MIT and a PhD in Computer Science from Lehigh University. He has been the President of Mousley Consulting, Inc. since its founding in 1993 and has directed the company's efforts in the areas of clinical database design, data editing/cleaning, document management, and submissions.

Karl Mousley received his BS in Mechanical Engineering from Rose-Hulman Institute of Technology and a MS in Computer Science from Villanova University. He has been a senior member of the technical staff at Mousley Consulting, Inc. since 1993. Among his significant accomplishments are the investigation, evaluation, and implementation of new computer technologies for clinical data management systems and developing strategic plans for integrating these technologies into current systems. He has extensive experience preparing Standard Operating Procedures (SOPs).

¹⁰ eTrials (2002a). <http://www.etrials.com/>. eTrials helps companies in the healthcare, pharmaceutical and biotechnology industries to simplify their data collection processes and to speed the results of their clinical trials.

¹¹ Oracle Clinical Remote Data Capture. Oracle White Paper

¹² eResearchTechnology, Inc. www.ert.com

¹³ Intrasphere Technologies, Inc. *Implementing Electronic Data Capture to Achieve Maximum Value*. www.intrasphere.com

¹⁴ eTrials (2002b). *eTrials and Arracel Reach Merger Agreement*. <http://www.etrials.com/10-15-2002.htm>.

Available **EDC In Depth** Research Reports related to this issue:

9.1 "EDC Vendor Analysis: Staying Strong During Market Turmoil"

In the current market of 60+ EDC vendors – including many unprofitable vendors whose products are not fully matured – it can be challenging for biopharmas to select products that will endure. In this report, we present both the risks and rewards associated with particular types of EDC service providers. Only with this type of analysis can biopharma companies select the best-suited, most cost-effective, and least risky vendors and products for their organizations.

9.2 "EDC Vendors In Depth: Electronic Contract Research Organizations (eCROS)"

By partnering with Electronic Contract Research Organizations (eCROs), sponsors are able to deflect some of the risk of running clinical trials, though at some financial and logistical cost. In this report, we evaluate the risks and rewards unique to eCROs and highlight specific vendor solutions, such as those offered by Target Health, Inc., PharmaNet and Datasential.

9.3 "EDC Vendors In Depth: Application Service Providers (ASPs)"

Application Service Providers (ASPs) offer sponsors the option of contracting out some of the more costly and time consuming aspects of clinical trial management, notably the hardware and software systems. In this report, we describe the typical ASP data center and provide an in-depth evaluation of notable vendors, including DataTrak, CB Technologies, and ETrials.

9.4 "EDC Vendors In Depth: Bringing Products In-house"

Choosing to bring and manage EDC systems in-house offers biopharmas great freedom and flexibility, but with significant risk. In this report we outline the steps necessary to bring EDC solutions in-house, with a special focus on minimizing risks and maximizing gains. Our discussion includes details regarding necessary internal support (e.g., IT and training), a description of legacy CDMS-based systems and bridges, and a detailed evaluation of specific EDC solutions, including Oracle's Remote Data Capture (RDC) and eResearch Technology's eDataEntry (eDE).

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