BY DENISE MYSHKO

The Continuing Evolution of

Paper may still reign supreme, but **THE EDC INDUSTRY IS COMING OF AGE.**

There is widespread agreement — at least intuitively — that the use of **AN ELECTRONIC DEVICE OR SOFTWARE APPLICATION THAT ALLOWS DIRECT DATA ENTRY** into electronic format **HAS THE POTENTIAL TO REDUCE TIME AND MONEY** within the drug-development process.

Dr. Paul Bleicher

THERE IS A LOT OF BUSINESS PRACTICE SOFTWARE AVAILABLE TODAY that can create common communication protocols allowing software systems to work together.

THE SOLUTION PROVIDERS

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ED BRYANT. VP, biostatistics and data operations, Purdue Pharma LP, Stamford, Conn.; Purdue Pharma is a privately held pharmaceutical company known for research on persistent pain and associated treatments. For more information, visit purduepharma.com.

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EDC

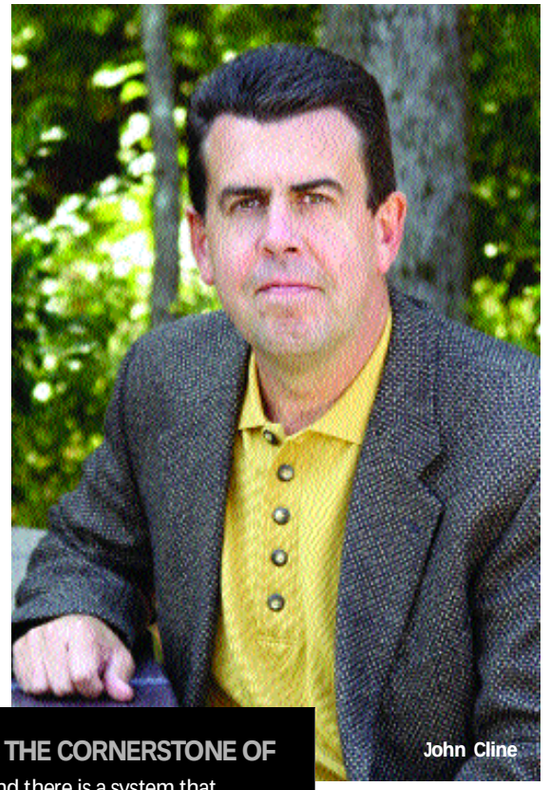
Despite efforts by some pharma companies and many suppliers, the paperless clinical trial has yet to become a reality. According to a recent Forrester Research survey of 400 CRAs and CRCs on current data capture practices, 97% are done via paper, 50% are through remote data entry, 35% are through scanning/fax, 25% are Web-enabled, 22% are through voice-response systems, and 5% are through a PDA.

Companies such as Merck, Pfizer, and Novartis have made a commitment to electronic data capture. Still others are experimenting with EDC and other technologies for automating clinical trials.

In 2002, just 8% of clinical-trial starts used EDC, although this is expected to increase to 33% by 2006. According to one recent survey, 48% of companies are using EDC in 10% to 15% of clinical trials.

While there have been some early adopters, for the most part the use of EDC among pharma and biotech companies has been limited. For one thing, EDC is a maturing industry and the tools that give pharma companies and CROs what they need are just now coming into their own.

The experts with whom PharmaVOICE spoke agree that the benefits of EDC include: improved data validation, quicker time to database lock, faster executed trials, lower monitoring costs, fewer queries, and no double data entry. These same experts say, in the future, data capture in clinical trials will be just one part of a larger process. Electronic data systems will need to be integrated with other systems to provide a comprehensive solution for clinical-trial management. To find solutions to streamline drug development, it will require a partnership among pharma and biotech companies, CROs, and IT suppliers.



John Cline

IF EDC IS VIEWED AS THE CORNERSTONE OF DATA COLLECTION and there is a system that integrates technologies to get a complete picture of the clinical trial, this becomes a very compelling argument for adoption.

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Glen de Vries

The Continuing Evolution of EDC

MACKEY. Data capture is evolving. We have seen the process move from double-data entry to remote data capture to fax/OCR and most recently electronic data capture. There have been gains in each evolution that ultimately aided in improving quality, time, and/or cost. The early versions of EDC were more of a store-and-forward approach or traditional RDC. Data were entered at the physician site and uploaded to the sponsor system. Although better than fax or OCR, this method still had multiple disadvantages, including data reliability and synchronization issues resulting from keeping databases in two separate areas. These disadvantages are being addressed as the speed of the Internet improves, which in turn will result in potentially significant savings. The next phase of EDC may involve an alternative to the way that data are captured. I would call it the direct data capture method or the Nirvana of data capture. This would involve two major components. The first would be to imbed the CRF design and patient schedule into the healthcare clinical system. The second component would be to capture the CRF patient data directly from the patient's electronic medical record (EMR). This would enable information to be sent from the patient's chart directly to the sponsor. This method has some patient confidentiality issues that will need to be solved before it is implemented.

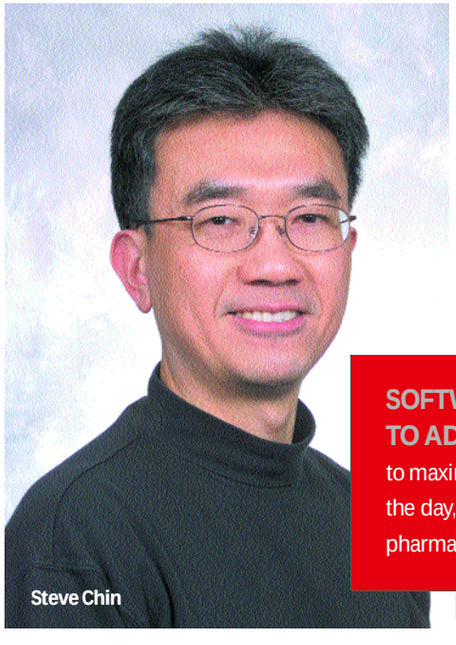
LANGFORD. The next evolution is that EDC will become a part of the data management of the drug-development process. EDC is just the first step in a large process. Electronic data capture is just one small part of data management, and data management is one part of drug development. There are a lot of other processes that are involved. A single EDC supplier probably can't solve all of the pharma industry's issues.

DE VRIES. The next phase is going to be eCDM, electronic clinical-data management. A lot of people will consider eCDM as being multiple systems that are bolted together. But that doesn't make the process more efficient. We view eCDM as a holistic system-approach to drug development. Typically data-management practices are set up around a protocol — eCRF design, edit check design, programming, and so on. Data management oversees the process of that data collection, facilitates double-data entry, reviews data, and resolves queries. Data management locks the database and creates deliverables that go to the biostatistics groups and then to the electronic submission publishing groups. An eCDM solution accomplishes all those things — one system that allows for a streamlined, controllable, and reportable workflow. That generation of product is emerging now.

A SPONSOR HAS AS LITTLE CHANCE OF SUCCEEDING IN A VACUUM in defining how EDC should work as an EDC company succeeding in trying to develop a drug. We all have to work together to achieve common goals.

MALOFF. In the long-term, I think there will be no "EDC" companies. EDC services will evolve to become part of a broader solution to accelerate trials and transform clinical-trial management. Five years from now, instead of EDC companies, there will be companies that provide integrated trial-management services.

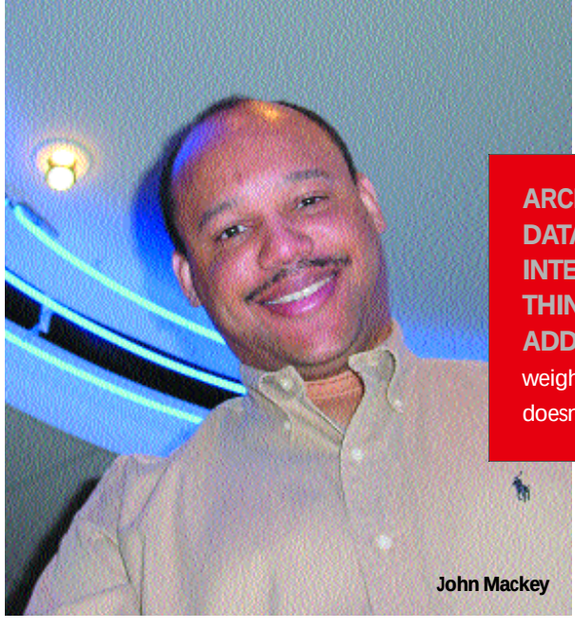
GREY. Down the road, large EDC companies and pharma will be planning for greater integration of electronic data capture platforms, data-management platforms, front-end and back-end platforms, and clinical-trial management systems, and these will tie into safety reporting systems. Eventually, there will be one-stop shop systems.


Steve Chin

SOFTWARE HAS TO ALLOW THE CUSTOMER TO ADDRESS AND IMPROVE PROCESSES to maximize the capability of the software. At the end of the day, there are two things very important to the pharmaceutical customer: cost and cycle time.

BLEICHER. Some EDC companies are not going to have what it takes and these companies will disappear. They're not going to have the critical mass of customers, and they're not going to have the technology that works. The companies that will survive will have the critical mass to develop not only a high-quality solution but also an integrated solution so that pharma and biotech companies can have the full power of the flow of electronic data.

HOFFMAN. It is unclear what the next phase of EDC software will be. But what may be successful is the transformation of EDC from "capture" to "communication." One can suggest that all implementations of current EDC systems move the task of data "keying" from trained dedicated staff in controlled environments, to medical professionals in potentially cramped medical office settings. This has obvious drawbacks, such as potential delays in getting the data entered and requirements for additional paperwork. The delays occur because entry is not often done at the time of the patient visit. More typically, entry is done when enough patient visits have accumulated to justify sitting down and "relearning" the system and entering the data. Most implementations of EDC use workbooks into which chart and other data are transcribed before entry into the EDC system. While this makes the data-entry process faster, it introduces an additional step in the QA process, a check of


John Mackey

ARCHIVING, SECURITY, PRIVACY, DATA AUTHENTICATION, DATA INTEGRITY, AND VERIFICATION ARE THINGS ANY SYSTEM SHOULD ADDRESS. Any tool that is worth its weight has to address those things. If it doesn't, it won't survive in the market.

the data against the chart and the workbook. With edit checks on the data at the time of entry, this usually results in cleaner data getting to the sponsor than in paper-based systems. But the delay in getting the data, and thus the ability to use EDC for timely trial management and critical path decisions, is compromised.

BLEICHER. There are a number of ways to think about integration. One is to integrate through Web services. The Web is a powerful technology that allows systems to be integrated more or less independent of the way that single systems are constructed and allows for legacy issues. When these systems work together, it doesn't mean that the software has to be built the same way. One system has to be able to send data and the other system has to be able to receive data. There has to be an exchange without the need for people to define what data are being received and where data should go. That is absolutely doable today and it can be done in a scalable fashion.

HOWELLS. We believe the more integrated a system is, the better. And by that I mean integrated rather than interfaced. Integrated means there is one store of the data within all systems accessing that data. Interfaced is where there are separate data stores and then there is software that frantically tries to keep them in sync. Most of the vendors who talk about integrated solutions actually have interfaced solutions. This means there are two copies of everything and pharma companies have to set everything up twice and then reconcile the data. Questions come up about which system will update the data, which will route it, and which one closes the data. Those control issues can get messy. What happens is that there are a lot of highly paid technical people trying to resolve these issues, and the benefits of removing the paper system are lost.

BLEICHER. What's becoming more apparent is the value of clinical-trial management data systems. CTM systems run the gamut of site management and patient management, through sophisticated operations management. The power of EDC is that the software collects information not only about the data but also about who entered the data and when the data were entered. It now becomes possible to manage the operational aspects of the trial, what sites are doing when, and how long it takes from one event to another event in the workflow of data management. All of that is available from electronic data capture systems and can be reported on in such a way that pharma companies can benchmark and improve processes.

DE VRIES. I don't think the integration issue is a hurdle that we can't get over. But I would not suggest that a large pharma company or even a small company try to implement a fully integrated solution in a single step. What can companies do to succeed the first time? Something simple. Use a single system in a context where the ROI goals are clearly defined. But at the end of the day, once a company has successfully run an EDC pilot or a couple of EDC pilots, it will have to integrate double-data entry and other paper-based data with the EDC data.

CLINE. The next phase of EDC is putting the tools in the hands of the people who can do the work. EDC could be seen as an island unto itself. For example, a software system should be able to integrate interactive voice response technology. This same system should be able to integrate lab data so doctors don't have to

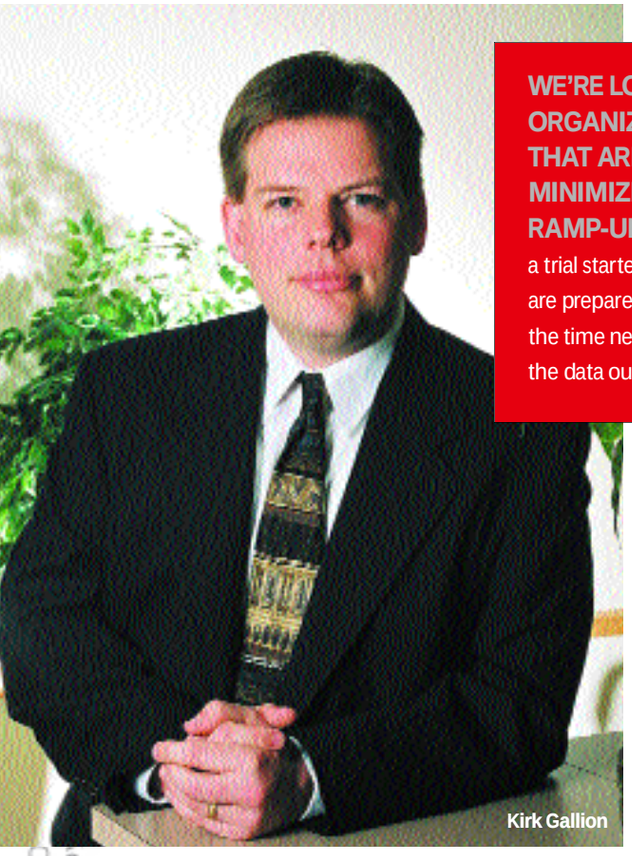

James Langford

IT IS IMPORTANT TO UNDERSTAND THAT EDC ISN'T REALLY ABOUT TECHNOLOGY. It's about processes. And processes are about workflow and communication. EDC companies are building products that will help improve business processes and enable companies to better manage their business processes.

Merck's Experience with EDC

Merck worked with DataLabs Inc., a developer of Internet-based applications for clinical trial automation, from October 2002 to May 2003 to measure the value of electronic data capture systems. The companies measured resources used, in full-time equivalents, as well as how many hours it took to accomplish certain tasks. The research also evaluated the cost of the software, as well as the training and the effort involved to put the processes in place. With EDC, Merck experienced:

- 70% reduction in data review time.
- 60% improvement in cycle time from last patient visit to locked database.
- 34% reduction in study design time and set up.
- 22% net savings on data-management costs. This is based on reduction of full-time equivalent costs (FTEs) and lower FTE costs (nontechnical users) on a per study basis. If average data-management costs are $500,000, savings of about $100,000 per study are achieved.
- 6% savings on overall study costs. This is based on fewer FTEs, not soft avoidance costs. On a typical $5 million study, this would be a savings of $300,000.


Kirk Gallion

WE'RE LOOKING AT ORGANIZATIONS THAT ARE MINIMIZING THE RAMP-UP TIME to get a trial started and that also are prepared to minimize the time necessary to get the data out of their system.

enter information from a paper lab sheet. And an electronic feed from the lab should be able to prepopulate a case report form. Some vendors are able to incorporate these different feeds. If the EDC industry can give a complete offering, that may cause some uptick in the adoption rate.

VARANO. The next phase will be to simplify the data-entry requirements at the investigative sites. This will be accomplished through EDC systems that are designed with the objective and priority on high site acceptance. Innovation in technology will allow for the development of EDC applications to replace current paper source requirements — folders and clipboards — with electronic tablets in a wireless Internet environment.

DAVIS. The next phase will be what I call "patient-centric" data capture. Looking at the pipelines of the major pharma and biotech companies, the disease areas in focus require information that comes directly from the patient — data about how they feel about their condition, their symptoms, their analysis of pain and discomfort. As a result, companies will have to communicate directly with the patient to collect data in a compliant and accurate manner.

MERLINO. Currently, EDC is just mirroring the data entry that's done on the back end. The site has become a data-entry operation as opposed to collecting medical data. I think the next capability will be collecting medical records directly from the source. This is called e-sourcing.

GREY. The next new thing is going to be capturing data in the exam room. Automation will continue, and be miniaturized. Right now, a doctor writes notes in a patient file and then someone has to pull those notes and put that information into a system. I see the use of e-diaries and hand-held devices exploding.

THE ULTIMATE NEXT STEP is to integrate electronic medical records and data coming directly from the labs and doctors' offices, bypassing traditional data entry.

HOWELLS. We see the use of wireless devices at the point of care increasing so the data don't start life on a piece of paper. But we have to be careful because healthcare information is highly fragmented. Companies are not going to be able to walk into a hospital and plug into that hospital's electronic medical record clinical-trial database.

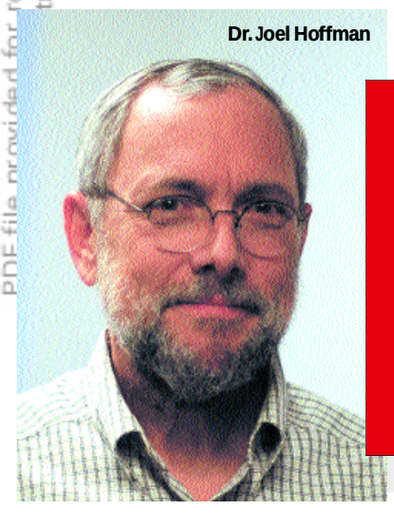
VARANO. Real-time analysis of clinical data is what EDC should be able to accomplish. My view is that the industry is moving in the right direction, and now has the necessary tools in place to accomplish this. But the focus needs to be in perfecting the processes. For example, more effective capturing and editing of the data at the site is critical. EDC is doing this successfully, but the goal must be to get the information into the EDC application at the point of patient interview. Until that happens, the focus and process need to encourage the entry of data immediately after the capture of data at the source.

MERLINO. To get to e-sourcing, the sources of data — the lab, the hospitals, the doctors' offices — need to get to a level of technology and capability where they are collecting their medical records in a format that the EDC vendors can then integrate into their solutions. The main problem is that all the labs are not automated yet. The doctor's offices are not all automated yet. The hospitals are not all automated yet. The EDC vendors are limited as to what they can do because they're dependent upon the sources of the data coming in electronically. This is starting to shift.


Paul Merlino Jr.

MALOFF. The next phase of EDC will go from proof of concept to resource-allocation integration. In other words, right now pharmaceutical companies are asking whether they should do EDC for a specific trial. The next phase will include a preferred partnership with an EDC provider just as we see with CROs. The EDC company and the pharma company will sit down on January 1 and determine which trials are "EDC-able" and formulate the action plan to ensure success from designing eCRFs through conducting the trial and locking data.

DE VRIES. There needs to be an approach


Dr. Joel Hoffman

THESE SYSTEMS ARE OFFERING THE GREATEST BENEFIT in not only providing timely clinical data, but enabling the more efficient management of trials, trial budgets, and clinical supplies.

where the vendor works in partnership with the sponsor in a risk-share environment. It's of benefit to both the sponsor and the vendor to continue that close working relationship because the sponsor is going to have a better chance at succeeding. If they share the implementation risk with the EDC company, they are going to benefit by helping to further define the problem areas and look for areas where EDC companies can help streamline solution implementations.

GLIKLICH. Sponsors aren't going to fall for gimmicks. What sponsors are looking for is a company that has experience and success in both the phase and therapeutic area that they are working in. If sponsors see a company that has proven success, they're going to move forward with EDC.

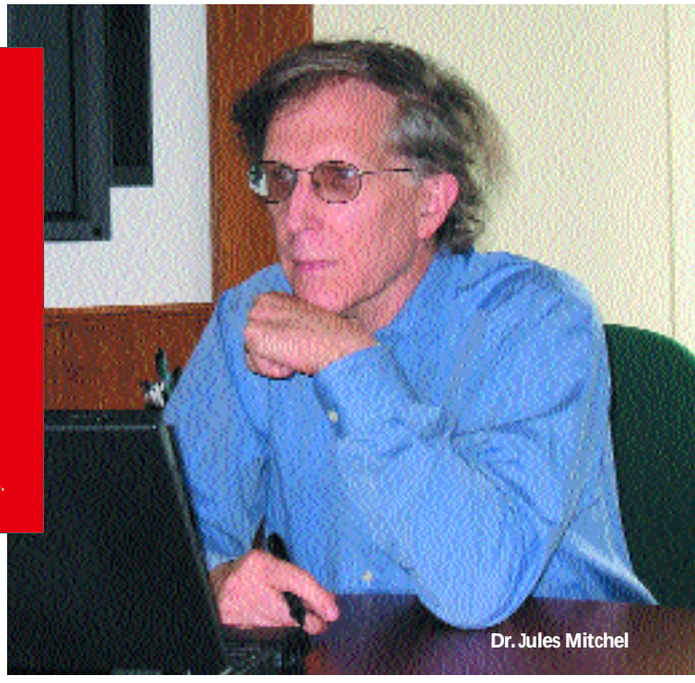
HOWELLS. EDC systems should be able to accommodate all of the data of a clinical trial. They should allow interactive data entry, and be able to collect data, including lab data electronically; they should have an integrated dictionary encoding system; they should be able to handle randomization; and they should be able to handle administrative functions, document tracking, and supply tracking.

OVERCOMING HURDLES AND BOTTLENECKS

CLINE. It's easy for the pharma industry to point the finger at the EDC sector and say that it is not ready for prime time when, in fact, it is the industry that is not ready for prime time. The pharmaceutical companies aren't ready to adopt. And this is because of the huge cost of business process re-engineering. It is not about the cost of software. It's about the cost of redoing business processes to take full advantage of what technology can do. EDC can only overcome resistance when pharma lets down the wall and lets us perform. Granted, the industry is littered with horror stories involving EDC. Change is a difficult thing. Until there is a compelling reason to change, people typically don't. Certainly the financial impact of developing a new drug — more than $800 million now — will cause a shift in the way companies do clinical trials. In addition, regulatory pressures are going to cause the industry to do some soul searching in terms of technology.

DAVIS. EDC technology is not the issue; the problem is how companies are trying to implement the technology. People forget that the clinical-trial process was conceived, designed, and refined using paper as the medium for collecting clinical data. As a direct result, SOPs and roles have solidified around the central need for paper. EDC and related e-clinical software technology changes all of this.

IN THE SHORT TERM, PHARMA COMPANIES ARE GOING TO WANT A SYSTEM THAT IS AUTOMATED and easily configurable. Pharma companies are going to want to have an automated system by which they can relatively quickly design the study, generate the forms, and enter all of the information and analyze the data. In the long term, integration will be key so that the data are only entered once, and the system knows where the information goes.


Dr. Jules Mitchel

GOODWIN. Probably the biggest hurdle is scale. Everyone has a failed pilot. Many companies do EDC and throw lots of resources at it and are not able to incorporate it into their operational models. I think the difference with Pfizer is that we've been able to achieve organizational change. The company has built business processes around the technology. We don't let the technology drive our business process decisions.

BRYANT. Purdue is growing quite rapidly. As the company has grown, we have recently begun to consolidate capabilities that larger companies probably had in place for a while in


Tony Varano

SPONSOR ORGANIZATIONS MUST BE COMMITTED TO CHANGING THE PROCESSES TO FACILITATE EDC TRIALS. This involves top management and the clinical team, and retraining to conduct EDC trials. Selection of an EDC solution should be driven by site-user expectations and not be the most technologically integrated software.

terms of in-house data management systems and in-house reporting analysis. That has set the stage to look at how we capture data from outside the company. On the immediate horizon is to be able to electronically capture data that aren't necessarily at the clinic site, such as laboratory data, EKG data, and diary data. We are buying a software system and doing system development work to configure that with our Oracle Clinical system. From there, we will look at the idea of developing a portal for data and the use of CROs. We view this as having value and may make the CRO solution a more attractive option for us to accomplish our clinical-trial work.

CLINE. To date, the pharmaceutical industry is very siloed in its approach, and isn't ready to adopt electronic data capture in a full-scale fashion. But that's not the fault of any one group within major pharma. Departments don't cross share with other departments, although I think that is beginning to change. Up until now, there have been many other stakeholders who have different needs and different agendas. To get people to make a unified commitment takes leadership from the top.

GREY. The biggest hurdle in this whole initiative is change management. There's no question in my mind that everybody wants to modernize and automate but first they have to change a lot of highly ingrained processes. In a big pharma company that sponsors a lot of trials, there are all types of processes and many people in place to do much of what EDC should help them do. There's a lot of pain to go through as they make that change.


Keith Howells

I THINK THE STANDARDS ISSUE IS AN EXCUSE because standards-based software already is available. The lack of standards should not be a constraint on collecting the data itself.

MACKEY. EDC is more than a software decision. It involves people, processes, and technology. The technology component has evolved to address the major issues of quality of data, time, and costs. The leading surveys indicate that most large pharmaceutical companies are using EDC technology in simple, early-phase trials and reserving old paper-based methods for large, complex Phase III international and multicenter trials.

GALLION. Very few systems meet our needs. The reason is that technology vendors are hyperfocused on one segment of the R&D process and they often develop tools without regard to upstream or downstream events. What ends up happening is that once the data are captured, companies have problems getting the data out and using it the way they need to. We frequently have to retool or help organizations with work-arounds to get the data ready for actual submission deliverables. No one plans on these work arounds.

GOODWIN. Scale matters. Being a large organization, Pfizer is able to take advantage of cross-site learnings as well as learnings from an international perspective. Pfizer can leverage these learnings and address areas that are not part of its core competency.

CHIN. To break through the pharma companies' hesitancy, the EDC industry needs to establish a very quick win. Companies have to focus on bottlenecks. One of the major bottlenecks is data integration — all the way from lab data to trial data. There needs to be an interface with the investigator, the sponsor, and the CRO. Technology alone is not going to solve this problem, but by finding the right balance between processes and technology, we believe it can.

DE VRIES. The vendors need to listen to the sponsors and the sponsors also need to listen to the vendors. We all have our core competencies. If we define our goal as eCDM and the specific return on investment — shorter times to market, lower cost for drug development, better visibility of trial or compound progress — we can now look at where we can provide better efficiencies to the sponsor company. We can work together to find those problem areas and to attack them and create integrated solutions.

BRYANT. There is a maturing of the technology and business value of EDC on the pharma side. Pharma companies that want to implement a very broad solution look very closely at how viable a company is, especially vendors that have a very uncertain economic base.

LANGFORD. When EDC first became available, pharma companies were reluctant to accept the software. Pharma companies are conservative and they were not going to put their critical processes on unproven software. This forced EDC suppliers to adapt a different business model than they originally intended, which is an outsourced service model. Now pharma has accepted that EDC does provide value and would like to scale to a larger number of studies. Companies are looking at the technologies available for large scale-up. But there are very few software applications that pharma companies can own and adapt to their processes that also can integrate well with their other legacy systems.

CHIN. One area that is important to address is the business model of the pharma company. Based on our observations and some of our relationships with major pharma, what pharmaceutical customers are really looking for is a process-based solution. Customers, particularly the larger ones, are looking for an integrat-

ed solutions package and are engaging in outsourcing of technology solutions.

MITCHEL. There are two levels of change for sponsors. One is to restructure the way pharma companies do clinical research. With EDC, pharmaceutical companies now have to do all the planning up front. And they have to do this by involving clinical, data management, biostatistics, regulatory, QA, and IT. This is a different work structure for a lot of companies. The second level of change is that some of the systems that companies currently have in place, and for which they have invested very large amounts of money, may have to be looked at and perhaps even scrapped. EDC may replace some of these systems and the way data are handled internally. Small eCRO-type companies that know drug development may really get it to happen. That is the story of the Internet. For example, in addition to Internet-based clinical trials, we are also building a relatively simple document-management system that could replace some elements of the high-end systems.

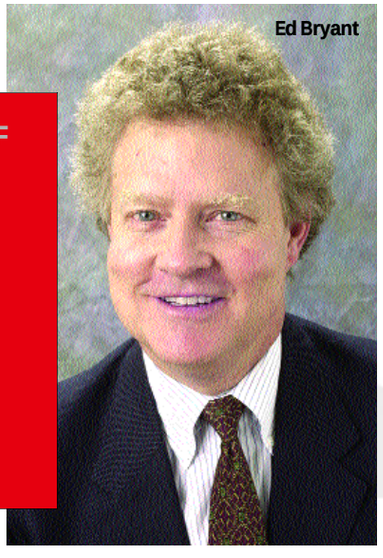
GOODWIN. The industry has been slow to adopt technology solutions, but this is not about technology. Companies care about the data captured in the clinical trials. We care about the information. We have to be comfortable with the technology, the infrastructure of a Web process, and the services provided to the investigator sites. But the integrity of the data is key.

MALOFF. The adoption rate that we see published by CDISC and CenterWatch is that EDC is currently used in about 25% of trials. That number is probably inflated because those data include interactive voice recognition systems and handheld patient diaries. It's not really electronic data capture, as I would define it. I think EDC is used in about 10% of trials now and will expand to more than 50% of trials.

HOWELLS. The pharma industry has been slow to adopt new technology, but that's not all its fault. A lot of the solutions have not been as good as they first appeared. The process of picking an EDC system, conducting the training, configuring the system, picking the study, rolling out the study, collecting the data, collecting the metrics, and evaluating the results can take at least 18 months. Then, if a company finds that it picked the wrong system, it has to go through the whole process all over again. A lot of the solutions have not been as complete, robust, secure, or user friendly as people first thought. There have been a lot of false starts that would have been hard to predict up front.

GREY. EDC software is still maturing. The concern that I hear in the marketplace is about a software's ability to handle multiple protocols, multiple trials, and other needs across an entire enterprise.

MERLINO. Electronic data capture software has a few issues. One is that it doesn't take into account that investigative sites have different capabilities. Those capabilities may not accommodate an EDC solution, a Web solution, or a remote solution. The site may be set up only to do manual processing of paper forms. Sites may not have the equipment, the connectivity, or the staff to accommodate EDC solutions.


Ed Bryant

EDC IS COMING OF AGE. There has been hesitation by pharma companies in adopting new technologies. But that is normal in a complex environment, especially considering how fast things can change.

DE VRIES. The early EDC adopters were working with tools and companies that didn't provide a lot of flexibility. Not every company is going to have the exact same workflow or the exact same data-management needs. That flexibility is a key piece in getting a return on investment. We are now seeing EDC companies that have the flexibility in their software and have the professional service organizations to help pharma transition to using their systems.

MALOFF. The adoption curve has been stubbornly slow. One reason is that there has been a lack of standardization. The FDA has not insisted that pharma companies get out of their comfort zone and into

Reasons for EDC Adoption Delays

	Biopharm	CRO
Regulatory concerns	53%	60%
Lack of clear technology solutions leader	51	51
Cost/Perceived cost	50	55
Inertia/Concerns about changing current process	49	57
Insufficient implementation of data interchange standards	59	50
Insufficient application features	47	43

Note: Results based on survey of 357 companies

Source: CDISC/CenterWatch Collaborative Research Project, 2002. For more information, visit cdisc.org and centerwatch.com.

Projected Global Trial Starts Using Web-enabled EDC Capture, 2001-2006

Web-enabled trial starts	2001	2002	2003	2004	2005	2006
Phase I trials	126	261	514	934	1,510	2,141
Phase II trials	651	1,320	2,508	4,313	6,532	8,711
Phase III trials	387	802	1,581	2,871	4,642	6,584
Phase IV trials	20	43	86	164	282	427
Total Web-enabled trial starts	1,184	2,425	4,690	8,282	12,966	17,863
Web-enabled trial starts as % of total trial starts	4%	8%	14%	24%	35%	46%
Web-enabled trial as % of total trials	4%	7%	12%	21%	33%	

Note: Numbers have been rounded

Source: Forrester Research Inc., Cambridge, Mass. For more information, visit forrester.com.

EDC vs. Paper

Costs for a Hypothetical Paper-Based vs. Web-enabled Phase II and Phase III Clinical Trial in 2003

	Phase II Trial: 20 sites, 10 patients per site, 12-month trial plus data cleaning		Phase III Trial: 200 sites, 10 patients per site, 24-month trial plus data cleaning	
	Paper	Web EDC	Paper	Web EDC
Initial setup and training	$32,000	$32,000	$36,000	$36,000
Site Internet access	NA	$2,400	NA	$48,000
Monitor visits	$360,000	$240,000	$6,300,00	$4,200,000
Data entry by sponsors/CROs	$240,000	NA	$3,600,000	NA
Data entry compensation to sites	NA	$240,000	NA	$3,600,000
Data cleaning	$100,000	$20,000	$1,500,000	$300,000
Operational expenses	$732,000	$534,000	$11,436,000	$8,184,000
License and usage fees	NA	$600,000	NA	$2,500,000
Operational savings from Web EDC	($402,400)		$752,000	
Value of accelerated time to market	$23,777,000		$65,195,000	
Operational savings plus accelerated time to market	$23,374,600		$65,947,000	

Source: Forrester Research Inc., Cambridge, Mass. For more information, visit forrester.com.


Dr. Bruce Maloff

THERE IS INCREASING PRESSURE ON THE INDUSTRY to do things more effectively, especially with 18 major drugs coming off patent in the next five years representing more than $37 billion in sales.

EDC. But things are starting to change; the FDA is actively encouraging and giving preference to studies that are EDC-driven, and companies that use EDC are reporting that they are achieving significant results in getting to market sooner.

CHIN. There remain some misconceptions in the industry as to what EDC is and what it means. First, there's the issue of credibility. Many of the EDC vendors are very small and there are questions about whether they will be in business in 20 years. This is important because FDA regulations clearly indicate that the applications and solutions that support any type of submission have to be available as long as the data are needed. Then there is the related issue of an EDC vendor's funding source.

HOFFMAN. Significant advances have been made in "almost" eliminating paper from the data-collection and transfer process. The collection and communication of patient-reported outcomes data can be electronically transferred to sponsors. Similarly, IVRS and lab data offer virtually paperless flow. These systems are offering the greatest benefit in not only providing timely clinical data, but enabling the more efficient management of trials, trial budgets, and clinical supplies.

DETERMINING THE ROI

MERLINO. We found that a lot of the expense — about 35% of the budget — is in managing the investigative sites, the data collection, and the grant payments. If pharma can get the investigative sites to use more technology, that 35% might be reduced. The only way pharma companies can improve the return on investment is to better manage their investigative-site processes along with the data-collection processes.

DAVIS. It can be difficult to provide ROI with the implementation of EDC. The main problem is that EDC and related e-clinical technologies provide many qualitative benefits, such as improved data quality, reduced error rate, and increased data density, along with the quantitative benefits, such as time to database lock. It is challenging to compare these equally when paper does not provide any of the qualitative benefits but costs a lot less than EDC.

BLEICHER. We can show a direct ROI from lowered costs of monitoring, reduced costs of clinical-data management, and fewer queries. But I actually think that strict reliance on ROI alone is overblown. People talk about ROI a lot, but in fact, decisions are not based on ROI alone. Companies often expect ROI in the first trial. We tell companies that they really need to get comfortable with the technology and see how their processes can change and only then will they be able to measure true ROI.

VARANO. I think it is reasonable for the pharma industry to expect a reduction in costs when conducting an EDC trial. The implementation should be phased in and delivered in the same timeline as a paper trial, and the export of SAS data sets should be delivered a few days after the close/lock of the database. These objectives may not be accomplished for every company for its first EDC trial, but if the necessary changes to internal processes are implemented and management is committed to these changes, and if the changes are executed properly, the subsequent EDC studies should meet or exceed objectives.

MACKEY. Clinical trials take way too long. Analysts estimate that one day saved in the clinical-trial process equates to $1 million in sales. If EDC can save days, that gives a company a shorter time to market as well as a competitive advantage. The biggest issue right now is reducing cycle times and getting clean data that companies can use. I see EDC as being a facilitator in that process.

CHIN. Based on our statistics, roughly less than 20% of today's clinical trials are using EDC in some form. The upside potential for companies is huge. EDC has been well documented in terms of economic benefit. Jeff Green (President and CEO of Datatrak International) wrote a white paper comparing EDC versus paper, looking at costs across the board from Phase I to Phase IIIb. He found that with EDC there was a mean savings of 44% in cost. Based on project costs, he found that EDC is five or six times less expensive than the paper model.

HOWELLS. At a recent meeting, one of our clients compared a large paper study with a large EDC study. This client found that the cost of handling queries on the paper study was $400,000. The cost of handling queries on the EDC study was $20,000. A common metric we hear is that queries go down by 80%. If a company gets one-fifth the number of queries, and the cost of handling a query goes down by a factor of 4, the total cost can go down by a factor of 20.

GLIKLICH. Customers have reported that their cost per cleaned page drops 90% to 95% comparing paper with our EDC system. Companies should also see total data-management costs drop, depending on the size of the trial.

MALOFF. Companies try to compare paper costs with electronic costs. That's not easy because paper costs are so imbedded into the process of doing trials that companies don't realize what the paper costs are. Coming from a CRO background, I know the hours of time wasted each week in chasing paper; and time is ultimately the most important expense in a clinical trial.


Dr. Richard Gliklich

SOFTWARE COMPANIES NEED TO FOCUS ON A PARTICULAR CLINICAL-TRIAL SEGMENT and create a compelling success story. Sponsors will respond to focus, experience, performance, and success.

CLINE. Comparing ROI on one trial for outsourced electronic methods versus a paper scenario is easy. There is no paper to print. There is no need to ship notebooks. If pharma companies allow a vendor to assist in the re-evaluation of the process, they could reduce one of the largest cost items in a clinical trial: monitoring.

MALOFF. EDC is not just about saving three months at the end of the trial in terms of data lock, it should also be about accelerating the trial from day one. Through an EDC trial, there are opportunities to share best practices about patient recruitment. A portal could be used to get a dialogue going between sites so that they could share insights and accelerate the patient-enrollment phase. Another example includes implementing dose-ranging decisions. It can take weeks for a sponsor to gather the data from each site and make decisions about next steps. With electronic data capture, sponsors know about trends much more quickly because the data are virtually coming in real time.

A CALL FOR STANDARDS

BRYANT. Not having standards in place makes this riskier. Over the last few years, there have been significant advances in certain types of standards. In particular, standards are developing under the ICH data transfer. A number of these standards will lead to greater confidence for investing in one large system that will help the business.

Robert Goodwin

EDC REQUIRES A FUNDAMENTAL CHANGE IN HOW COMPANIES WORK. Organizations need to think about how they work in paper today and what the goals are for that organization in the future. For us, we're looking at bringing 20 new medicines to the market in the next five years. So, EDC would feed into our goals.

CHIN. Standards are big issues. Conducting clinical trials, pharmaceutical companies have to deal with a large number of internal and external data sources such as the study sites, CROs, and laboratories. It's not uncommon that each data source has its own proprietary systems and applications, and many are paper document-centric.

LANGFORD. It is important that the pharma industry embrace open standards. We believe CDISC is the right way to go. We have adopted the CDISC ODM standards. We use them internally with our product, and we use them as our connecting point when integrating with other systems. There are other companies in the marketplace that have a stake in their own proprietary ODM and resist accepting industry standards. That concept has to break down if we are to improve the way products are developed. The pharma companies have to be willing to accept and promote CDISC as a standard. Once that occurs, most of the issues and problems associated with integrating software can be resolved.

KUSH. Data standards are key, but first people have to get over a few more hurdles. They also have to start telling their vendors to use these standards. It's coming from the submission end, whether people like it or not. The FDA wants to be able to review these data better. The overarching goal is the safety and health of our population, to get safe drugs approved, and to identify the problems up front instead of putting drugs on the market that later have to be pulled. FDA wants to have these data in a standard format so that it can review them better when a submission is filed.

HOWELLS. Companies are not obliged to follow any externally dictated standards in collecting clinical-trial data. They can call things what they want. They can make up the rules for edit checks. The only standards they need are within a company. The CDISC standards are just starting to come into vogue.

Cort Grey

SOFTWARE NEEDS TO BE FURTHER DEVELOPED to offer multiple collection methodologies and multiple connectivity downloading capabilities because there are just too many variances across an enterprise.

GREY. I often see that pharma moves much more rapidly when there is a regulatory body that forces a decision. That's not really happened here. There is much talk about electronic source documents, electronic medical records, but none of the regulatory authorities make this a stipulation. It's not as top of mind as it would be if there was a regulatory body pressing for adoption.

GALLION. We're looking for vendors that understand that there's a larger spectrum to research. This is not just about whether a company has a responsive Web interface for the data-entry piece. We are looking for companies that are thinking about the eventual submission deliverables. Emerging standards like CDISC's ODM are going to help facilitate that.

BRYANT. Part 11 compliance is an issue. There are lots of interesting technologies that have been developed, but when evaluated more closely they haven't been developed with the rigor that we know has been the directive coming from the FDA. This really causes appropriate hesitation.✦

PharmaVoice welcomes comments about this article. E-mail us at feedback@pharmavoice.com.