Realising the value proposition of EDC

A review of the important factors to consider and steps to take in order to implement electronic data capture (EDC) successfully, and how to make the transition from slower, more expensive paper methodologies to technology-driven global clinical trials.

Dr Jeffrey A. Green, DATATRAK International, Inc

The experiences of pioneering "early adopters" have progressively solved many past limitations – both real and perceived – and are now bringing definable and significant value to their organisations

Over the past twenty years, there have been many attempts to advance the global clinical trials industry beyond manual handling of three-ringed binders of paper as the standard for data collection and management. For an industry that encompasses the sophistication of gene therapy and the risks associated with developing innovative treatment modalities as a daily routine, its hesitancy in advancing data collection and review beyond NCR paper, air travel to review information, "yellow sticky notes", manual "key punching" of data and the toleration of nine-month lag times for Query resolution, appears difficult to explain.

There are many reasons enumerated throughout this article that partially document why this seemingly logical transition towards technology – that took place in other business sectors decades ago – has lagged behind within the international pharmaceutical and medical device industries. Some of the reasons are justified, while others are not. Some excuses merely represent political protectionism within numerous departments by individuals who have delayed such advancements at the expense of their company's product development objectives. In order to avoid repeating the mistakes made by others, a careful and honest examination needs to be made of all these reasons along the road to achieving long-acclaimed goals of positively influencing the Quality, Time and Cost of getting innovative therapies and devices to market.

Despite the slower-than-expected corporate adoption of EDC (electronic data capture) worldwide as the new standard for collecting, reviewing and transmitting clinical trial information, this market sector has made significant advancements over the past several years. Specific to our Company, the growth rate in contracts has been more than eight-fold in three years. Simply stated, the quest for technology in all aspects of our lives – including clinical trials – means that EDC "will not go away". Successive approximations will continue until "the right process" and "the right technology platform" are found. In this respect, delays can be a valuable learning experience for those wise enough to observe. The experiences of pioneering "early adopters" have progressively solved many past limitations – both real and perceived – and are now bringing definable and significant value to their organisations. This article will summarise some of the key criteria and steps that have been instrumental in successful EDC deployments in over 40 countries around the world.

Quantifying the value proposition – what's at stake?

The three most important criteria to improve in any product development effort are Quality, Time and Cost. These three "metrics" have all been significantly impacted through the proper use of EDC. Moreover, these metrics have been substantiated by independent sources – the hallmark of verifying new concepts.

The initial public study of metrics with EDC was done by Banik *et al.* while at Bayer Pharmaceuticals in 1998 (1). These results are depicted in Figure 1. The long-stated but rarely realised goal of accelerating clinical development was shown to be an impressive 30% improvement over paper methods. Outsourcing – simply to another party, as with a Contract Research Organisation (CRO) – has not produced such results, since a change in process is required, not simply a different group deploying identical procedures.

Equally impressive were dramatic reductions in Queries (82%) and Query Rates (86%) through the use of immediate edit checks that are not possible with paper, and a significant reduction in the time to database lock (43%).

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The metrics representing Quality and Time were reproduced in 2002 by the data management department at Gilead Sciences led by Mr Adrian Hsing (2). Their data, derived independently four years after Banik's findings, was virtually superimposable, with a 75% reduction in Query rates and a 45% reduction in the time to database lock.

In order to quantify the economic value proposition of EDC versus manual methods, two other independent sources have produced surprisingly similar results concerning this parameter. Green (3) utilised the foundational data of Banik (1) and The Center for Drug Development and Research (4) to create a financial model for the use of EDC in an entire drug development programme. Cost-savings alone with EDC versus paper methodologies was calculated to be greater than $60,000,000 per drug.

Recently, Novartis Pharmaceuticals has documented actual savings of $65,000,000 in 2002 in substituting EDC for outsourced paper methodologies, previously done with CROs (5). This would have to be a minimum figure for savings with more modern deployment strategies, as the relatively outdated platform of required hardware deployment at every site continues to be burdened by accompanying logistics and excessive costs, representing significant questions about scalability and expense. Some have estimated such additional costs of a distributed model to be as much as $15,000 per site.

Neither one of these economic assessments included augmented revenue from a faster speed to market from an acceleration in development, nor did these assessments include savings from being able to cancel ineffective products based upon superior and timelier results. To accurately assess the full value of EDC, such figures would be additive.

Though it is stated by some that "we can't afford to do EDC", upon an examination of the data above, this statement should be rephrased to "how can you afford not to do EDC".

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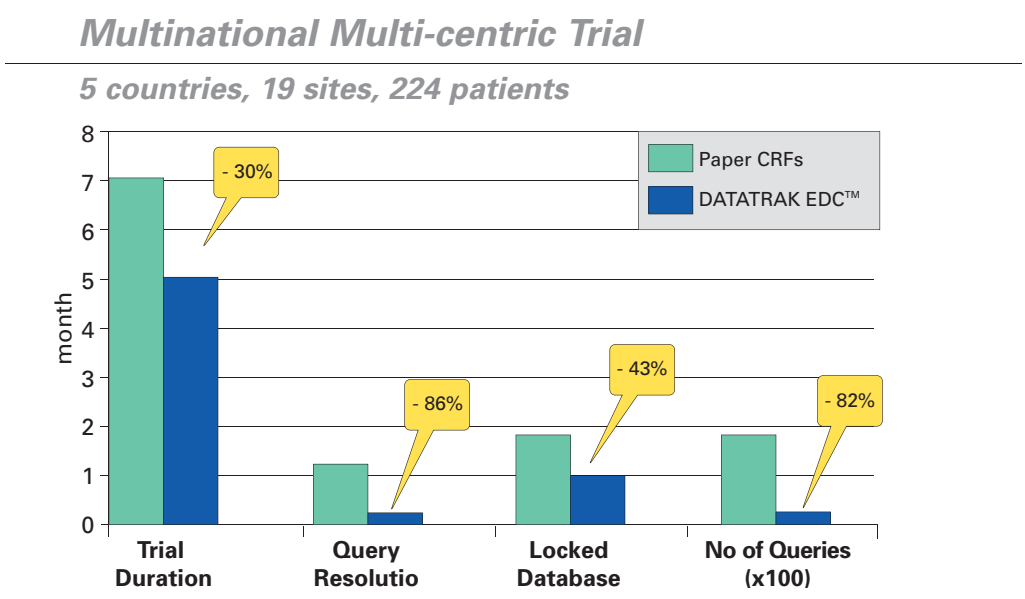
Figure 1. Results of the initial public study of metrics with EDC done by Banik *et al.* (1).



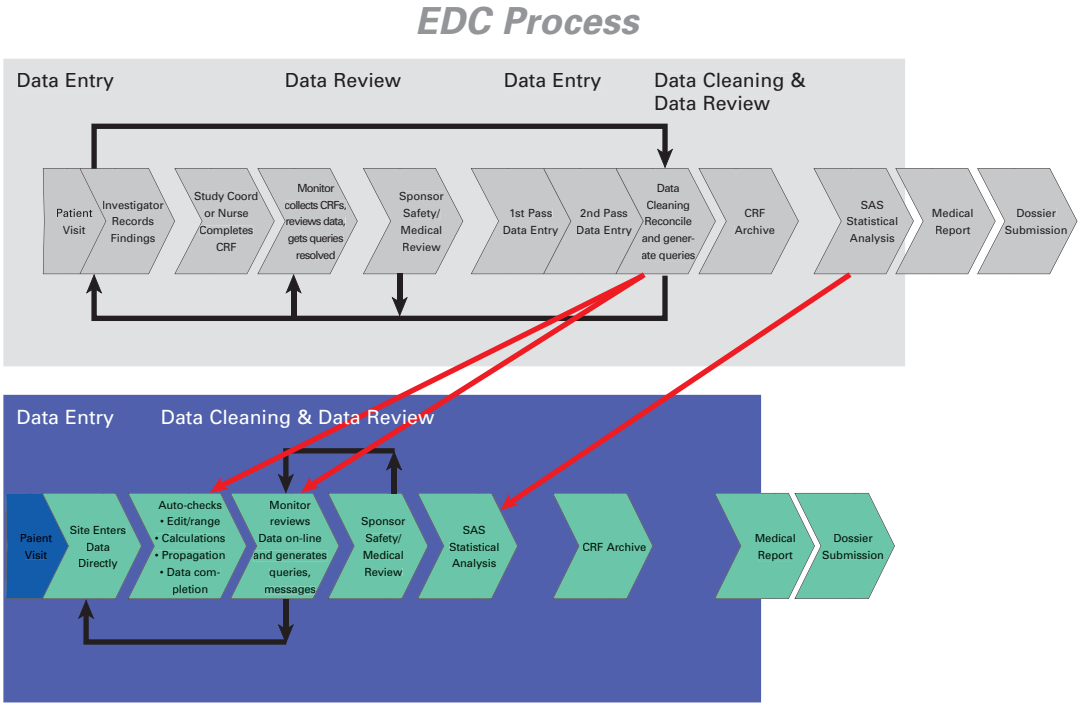


Figure 2. Steps to success with global EDC implementations.

It's all about process

The organisations that are optimising success with EDC have two major approaches in common: 1) they have selected the correct technology, and 2) they are gradually changing their process in moving to EDC. They are not simply "automating paper" and forcing future process to be driven solely by decisions made years ago on systems for manually handling data.

A poignant example relates to some companies that use EDC simply to feed into traditional "back-end" systems for the resolution of Queries – exactly as is done with paper. This "process" mitigates one of the major advantages of EDC and is classified by some as "getting your garbage faster". Under this scenario, the massive reduction in Query workload, and the accompanying economic and speed benefits do not exist.

Figure 2 summarises graphically how the clinical trial process changes with EDC and shows how accelerating the drug development process by 30% can be achieved and explained, step by step.

Vendors often have an advantage because of exposure to competitive intelligence from each customer. This can accumulate into a great deal of information. Close interactions with the "rank and file" almost always gravitate towards comparisons of competitor companies within a sector. While maintaining confidentiality, a vendor can learn which products and/or companies are good or bad, and the reasons for such classifications, based upon previous experiences. What is never discussed publicly is often elaborated upon privately.

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As a result of this learning process, which has intensified over the past several years as EDC has advanced, some of the factors which have been consistently predictive of success can be summarised; in addition, the reasons why some companies have had to revisit initial decisions, once thought correct, can be explained. Understanding the steps already trodden can be very valuable to companies that are currently considering EDC.

Predictive factors of success

Listed below are the top seven factors predictive of success with EDC accumulated from over 20 customers. Reasons related to each factor are briefly described. It is assumed that the most important factor of regulatory compliance with 21 CFR Part 11 can be ascertained by customer audits, and is not itemised. Factors listed are those that apparently are not obvious, as many customers have changed paths following initial choices of technologies that were incorrect.

Experience in global implementations and an approval pedigree Clinical trials are often international; it thus makes little sense to standardise on only a single continent solution. Bringing a product to market is the ultimate goal; thus, successful regulatory approvals where a software suite was used seems important. Additionally, since modifying processes is critical, the experience of the vendor can help in creating new "e-SOPs" for clinical trials. Companies should take advantage of this experience.

System performance at investigative sites worldwide at low bandwidths This is one factor involved with user acceptance; retarded performance breeds non-compliance. This can be easily

evaluated via dial-up connections on independent laptops, without the assistance of caching downloads during product demonstrations. Unwillingness by a vendor to do this is a tell-tale sign. This has been a common mistake of customers who selected product suites after presentations from C-drives, instead of demanding live performance via the Internet – the medium that would ultimately be used by their sites. Fancy marketing programmes do not change the laws of physics; subsequent performance problems, therefore, are not surprising. Remedies to compensate for these inadequacies result in increased customer expense.

User acceptance This includes system performance, workflow and user interfaces; this has been the main reason for EDC failures of the past. All vendors should supply independent assessments of user acceptance to customers. There must be a balancing of priorities between the "back-end" needs of data managers and "front-end" acceptance by investigative personnel. When one need takes precedence inappropriately, process becomes unproductive.

Diligent, field-based audit trail EDC audit trails should be superior to those with paper. Though many EDC systems are compliant today with audit trail tracking as in 21 CFR Part 11, many believe that diligence in audit trails will increase in future revisions (6).

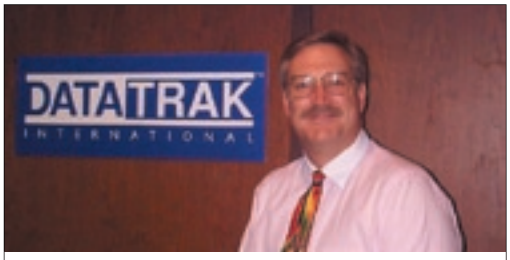
Transparent business model Data with EDC is more easily tracked; the same should be true of the financial aspects of software use in clinical trials. "Bait and switch" tactics should be minimised, as there is less room for cost fluctuation compared with manual processes of surprise expenses. Transparency allows for multi-year projections for entire programmes of development. Beware of licence models or fixed monthly payments, where costs are not directly proportional to the amount of work performed in a clinical trial.

Service levels (hosting, help-desk, problem-solving) Technology is a necessary but not a sufficient factor for success – this remains a service business. With EDC, service is now extended to investigative personnel worldwide (Internet connections, help desk and so on) and not just the clinical trial sponsor.

Software ease of use EDC is inevitable – just as email and Internet use have expanded worldwide. As comfort levels rise, sponsors will take more tasks in-house, much in the same way that the functionalities of Excel™ and PowerPoint™ have been internalised instead of outsourced. Therefore, ease-of-use and technology transfer will become critical decision factors in the selection of a product.

Conclusion

The advantages of EDC are unquestionable – if the correct product is chosen. Multiple independent parties have verified the advantages. Some excuses as to why not to use EDC will persist among select groups, but these will gradually dissipate with continued successful implementations. The value of reference-checking cannot be over-emphasised in attempts to bring competitive advantage to a product development company through the strength of technology.



Dr Jeffrey A. Green is the Founder, President and Chief Executive Officer of DATATRAK International, Inc, a publicly-traded, leading technology company in the Electronic Data Capture market (Nasdaq: "DATA"), with headquarters and global hosting facilities based in Cleveland, Ohio, and a European operations and software development office in Bonn, Germany. Previously, Dr Green was an Assistant Professor of Medicine and Radiology at Case Western Reserve University School of Medicine from 1984 to 1992, and has over 20 years' experience in the clinical trials area. He was responsible for directing over 90 investigations in clinical cardiology and PET-scan imaging prior to founding DATATRAK International, Inc. Dr Green has authored over 90 publications and has been an invited speaker at more than 170 national and international meetings. He is a past recipient of the McKeen Cattell Distinguished Achievement Award from the American College of Clinical Pharmacology. Dr Green can be reached at: Jeffrey.green@datatraknet.com

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