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05/2015 WHITE PAPER

Reducing the Time to Market with an eClinical System

The once slow march from paper to electronic data capture (EDC) for clinical trials has become a stampede. In 2000, virtually all trial data was captured on paper case reporting forms (CRFs). By 2013, 75 percent of new trials were conducted using an EDC system. Today the figure is even higher, especially for trials run by global pharmaceutical companies, for Phase III trials and for trials in the US, Europe and Japan. However, it's still not 100 percent.

This begs the question; why are any trials at all still conducted on paper?

Part of the reason may be that fast-growing biotech companies, medical device companies, smaller academic centers and investigators initiating their own trials still evaluate EDC solely on how much it will save them on the operational costs of conducting trials. For these agile sponsors, operational cost savings may actually be the least important benefit of EDC. The key benefit of shifting from paper data collection to EDC is slashing "time to decision" and, by extension, time to market.

By delivering more timely and accurate clinical trial information, EDC accelerates the decision-making process, allowing sponsors to get their drugs to market faster. This paper examines the key contributions an EDC system makes to accelerating time to market, including up to 41 percent faster study startup and up to 65 percent faster study close-out. In addition, the paper briefly touches on additional sources of time-to-market acceleration that are available by extending traditional EDC to a broader eClinical platform.

It's About Time

Roughly 15 years after the inception of EDC for clinical trials, the surprising fact isn't that more than 75 percent of new clinical trials use an EDC system. It's that nearly 25 percent still don't.

Are the sponsors whose studies still collect data on paper technology laggards? Hardly. Their numbers include, for example, many innovative pharmaceutical, biotech and medical device startups researching cutting-edge treatments spanning the range of therapeutic areas globally.

However, the business case for EDC in these agile life sciences companies is quite different than in global pharmaceutical companies. Large sponsors running many trials can easily justify EDC based on operational cost savings alone; treating accelerated time to market is a bonus. Emerging sponsors running only one or two studies may believe they will get less operational return on their EDC investment, or that EDC technology doesn't matter if they are outsourcing studies to a contract research organization (CRO). But EDC can dispel these assumptions by helping CROs and clinical sponsors realize multiple benefits in any type of use-case scenario.

When EDC was originally conceived, its value lay in replacing paper processes. This meant quality improvement and cost savings. Today, it's all about time to market. Because EDC allows agile life sciences companies to rethink the clinical development process, they can analyze study results sooner by reducing study build and database lock times.

Cloud-based EDC systems help by greatly reducing deployment time and cost, and by enabling sponsors and CROs to exploit a common platform. However, many emerging life sciences companies are more driven by speed than trial cost. For these companies the business case for EDC is that by delivering faster and more accurate information, EDC accelerates the decision-making process—allowing sponsors to get their drugs to market faster. When EDC was originally conceived, its value lay in replacing paper processes. This meant quality improvement and cost savings. Today, it's all about time to market. Because EDC allows agile life sciences companies to rethink the clinical development process, they can analyze study results sooner by reducing study build and database lock times.

What Is a Day Worth?

What difference does a day make? For patients waiting for life-saving or enhancing treatments, the answer is clear. The human value of a day or a month more of reduced symptoms or progression-free survival is profound.

Even in purely financial terms, the value for sponsors of time saved getting to market is substantial. For example, Gilead's Sovaldi, a new hepatitis C drug approved by the FDA in December 2013, grossed $10.3 billion in 2014. That amounts to $28.2 million per day.

For emerging companies betting their future on one or two compounds or a new device, the stakes rise all the way to company survival. Whether or not a new treatment is successful, the speed boost provided by EDC can help life sciences organizations outpace their competition by either advancing the treatment to the next stage or have it "fail faster"—enabling them to move on.

How Much Can EDC Accelerate Time to Market?

Although an eClinical platform can accelerate time to decision in a number of areas, EDC alone has the most impact in shortening study startup and study close-out by removing tasks from the critical path and eliminating the need for reconciliation. Based on 15 years of experience that includes powering about half of the world's EDC-driven trials, Medidata estimates that sponsors can:

- Accelerate study startup through a 27 percent to 41 percent reduction of study build time
- Reduce study close-out time by 41 percent to 65 percent

In combination, taking time out of a study startup and close-out can bring forward the clinical study report and regulatory submission date by up to 45 days. The next sections of this paper will explore specifically how EDC drives these two key accelerations.

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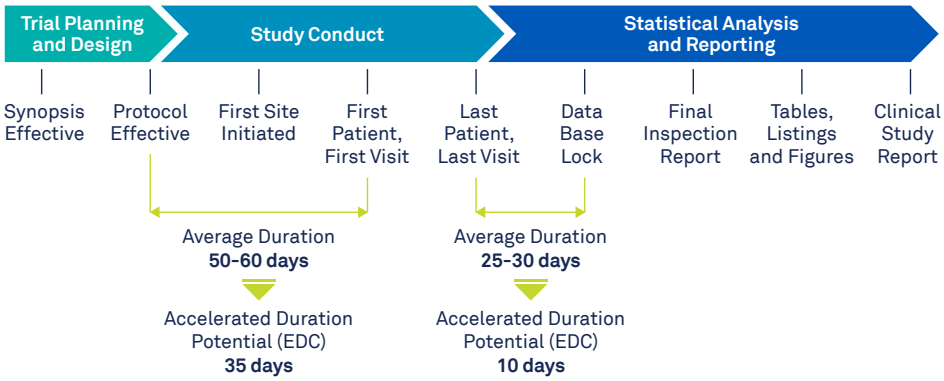
Figure 1: Clinical Study Process Cycle Time Reduction Example—Potential to reduce cycle time by up to 45 days



EDC Accelerates Study Startup 27–41 Percent by Reducing Study Build Times

Sponsors can dramatically reduce the time it takes to be ready for the first patient enrollments using technology. One of the best ways is to use EDC to get the clinical trial database in production prior to the first patient, first visit (FPFV). Based on sponsor interviews, a reasonable benchmark for database go-live is six to seven weeks after protocol finalization.

The big driver for this cycle time improvement comes from the use of company standards, mainly through the reuse of the electronic case report form (eCRF) global library. Adoption of these company-wide standards ensures reusability and consistency across studies, partners and internal teams.

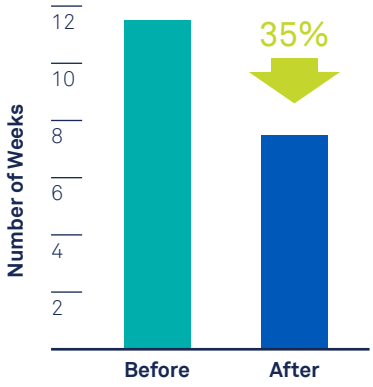
The initial configuration of EDC should be an exercise in creating internal standards. Once standards are created for forms and the associated edit checks, all elements can be easily reused for other studies through a global library system.

A new study can be created by merely invoking a copy function, which clones the established design to create forms for the next trial.

Case Example - Purdue Pharma Leverages a Global Library to Reduce Study Build Times by 35 Percent:

- Working with multiple CRO partners, Purdue needed to ensure clinical data standards were uniformly implemented while also minimizing EDC study build times.
- Tasked to build five Phase III studies in six months with rigorous timeframes from protocol approval to first patient in, Purdue developed its global library of data standards, forms and edit checks, which were available to be copied for ensuing studies.
- The initial global library consisted of 26 CRF pages and 520 standard edit checks as well as field checks, derivations, custom functions, data dictionaries and variables.
- Common design standards enabled the reusability of the eCRF global library, reducing database build times from 11–12 weeks down to 7–8 weeks.

Figure 2: Study Build Times



This company standardization allows the clinical group to create the CRF forms and—together with data management—deploy a full EDC study in days rather than weeks or months, depending on the complexity of the study and the experience of the EDC study builders. It also lowers the required programming experience level for form and data designers, allowing therapeutic area experts to create the EDC design with zero programming. Finally, it provides a consistent way to capture metrics on the study build, delivering additional ongoing improvements in efficiency.

The efficiencies of study reuse and metrics feedback vary between organizations but can lower implementation time, thereby eliminating the perceived advantage of a paper trial.

EDC Reduces Study Close-out by 27–41 Percent by Being a "Single Source of Truth"

Sponsors can dramatically speed up the time it takes to create the clinical study report (CSR). One of the best ways to achieve this is by using EDC to ensure database lock (DBL) quickly. Based on sponsor interviews, a reasonable benchmark for the time it takes to DBL from last patient, last visit (LPLV) is 10 days.

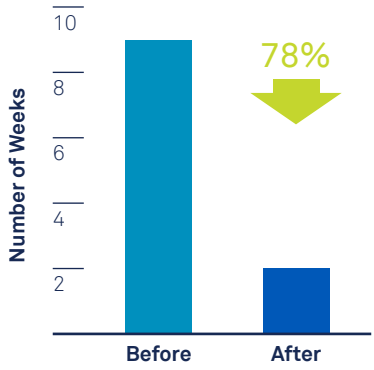
The speed at which data cleaning progresses and database lock is achieved impacts the submission timeline. The ability for EDC to be a single source of truth for clinical data enables cycle time improvement here. The process leading up to DBL is demanding, with the data management team under pressure to make sure all data entry is complete and finalized. All queries must be resolved and data cleansed. This process can last up to 12 weeks, from LPLV to DBL. Because analysis requires complete and final data, a few missing data points can stop the statistical analysis from progressing, leaving the statistical analysis team waiting to work on the clinical study report.

Because EDC captures the status of all incomplete forms, management reports can be used to drive the close-out of a study. This involves confirming when all forms are monitored and locked, and then automatically routing CRFs for signatures. Prior to locking the data for a patient, a final check can ensure that there are no unresolved edit checks and queries.

Case Example – Abbott Accelerates Study Close-out Cycle Time by over 75 Percent Using EDC

- Abbott introduced proactive correction of operational performance to reduce DBL delays, for example, by ensuring sites enter data within five days of patient visits and queries are opened within five days of data entered.
- Abbott reduced LPLV to DBL cycle times on average from over two months to less than two weeks. Abbott made key improvements focused on data-cleaning performance tracking and elimination of duplicate effort by monitors, data managers, clinical safety analysts and biostatisticians.
- Introducing an Integrated Data Review Plan to aggregate all the data review and remote monitoring components into a single document, Abbott essentially created a guidebook to get the study team to DBL as quickly as possible.

Figure 3: LPLV to Database Lock



Beyond Basic EDC: Additional Time-to-market Accelerators

While adopting EDC alone can substantially accelerate study timelines, adopting an eClinical platform that unifies EDC with safety, monitoring, payment and interactive response technologies can shave weeks from the trial timeline. This approach can also save money and improve data quality. The following are just a few examples.

Example one: Reducing process and reconciliation time for serious adverse events (SAEs)

Many sponsors combine their EDC with a safety system. According to Medidata's analysis, this can reduce the processing of SAEs, including time-consuming reconciliation, by an average of 81 percent, taking it from 2.1 days to just 0.4 days, on average. There is a reduced risk too since the data is auto-coded.

Using this capability, investigators enter all SAE data directly into the EDC system, which then triggers it to be automatically transmitted to the safety monitoring system. Changes to the SAE for follow-up are highlighted with original data side by side. This saves the investigator hours of time completing forms and reconciling data.

Example two: Reducing data entry cycle-time

Across a number of studies, sponsors using integrated interactive response technologies from the same vendor experienced a 35 percent drop in data entry cycle-time (i.e., from 14 to 9 days) from visit to form completion. There also was an 83 percent reduction in setup time, going from 12 weeks on average to just 2 weeks, by using an EDC solution with interactive response technologies from the same vendor. This removed the IVRS setup from the critical path so that it did not impact the study go-live.

Example three: Reducing SDV without reducing quality

Based on analysis of 85 studies in the Medidata Insights® database, sponsors using an integrated targeted source data verification (SDV) and EDC functionality reduced the number of onsite monitoring days by 33 percent, going from 15.4 to 10.2 days per year with no reduction in quality (i.e., post-data correction rates). For one biotech sponsor, this lower SDV rate equated to a documented 30 percent cost savings ($2.5 million on a single study). Other sponsors reported clinical research associates (CRAs) could review and query data three weeks faster using targeted SDV plus EDC together, rather than just EDC. This left more time for the CRA to focus on value-added activities at the site.

Companies adopting EDC for the first time need not adopt a complete eClinical platform at once, but should include these future platform capabilities in their EDC selection criteria.

The Time Is Now to Capture the Full Value of EDC

So, once again, why are any trials at all still conducted on paper?

As this paper shows, there is significant value in EDC for growing biotech companies, medical device companies, smaller academic centers and investigators initiating their own trials. However, the business case for EDC for these agile life sciences companies is quite different than for global pharmaceutical companies. As these companies realize the large impact of EDC on slashing "time to decision" and, by extension, time to market, they will be more eager to adopt this technology.

What's more, EDC as the cornerstone of a broader eClinical platform can further accelerate time to market. Having the flexibility to expand from EDC into a broader eClinical platform over time helps any sponsor, as its capabilities expand and clinical development needs change.

About Medidata

Medidata is the leading global provider of cloud-based solutions for clinical research in life sciences, transforming clinical development through its advanced applications and intelligent data analytics. The Medidata Clinical Cloud® brings new levels of productivity and quality to the clinical testing of promising medical treatments, from study design and planning through execution, management and reporting. We are committed to advancing the competitive and scientific goals of global customers, which include over 90% of the top 25 global pharmaceutical companies; innovative biotech, diagnostic and device firms; leading academic medical centers; and contract research organizations.

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