The Clinical Trial Management System—The Central Intelligence Hub

Henry Levy



Henry Levy is the Managing Partner for Accenture's Life Sciences R&D Practice in Europe, based out of Zurich, Switzerland. Henry has worked in the Pharmaceutical Industry for the last 17 years, providing services across Strategic Consulting, Technology and Outsourcing to most top 20 biopharmaceutical companies. Henry has focused on helping sponsors achieve high performance in driving new therapies to the market. Henry is considered an industry expert in the clinical trial process and speaks often at key industry conferences.

E: henry.d.levy@accenture.com

Evolutions in technology, such as point-to-point data integration and centralized data capabilities, are enabling clinical trial management systems (CTMS) to increase the value they add as pivotal tools for streamlining clinical development operations. Accenture believes that collaboration functionality, bringing clinical trial stakeholders closer together, and the use of analytics to drive improved insights into the clinical trial progress, are major drivers of the evolution in the CTMS environment. CTMS is in a prime position to support critical decision-making by becoming the central intelligence hub in an integrated eClinical system that serves the needs of all stakeholders in the process. Furthermore, Accenture asserts that CTMS will also support clinical trials of the future by offering greater insight into the drug development process.

The biopharmaceutical industry is experiencing a challenge; as research and development (R&D) expenditure within the industry has increased tenfold over the past twenty years the number of new drugs approved continues to be flat or, as is the case recently, to decrease.[1,2] Moreover, it is Accenture's opinion that the continued merger and acquisition activity will not be enough to address the long-term impact on the industry's valuation in the market. Therefore the situation has forced the industry to become highly focused on cost reduction.

Current clinical trials expenditure accounts for approximately 60 % of the total development spend, with the development spend itself accounting for 70 % of the overall R&D budget.[3] With 40–50 % of overall expenditure allocated to the clinical trial process,[4] the improvements in clinical trial execution and productivity, coupled with how clinical trials are managed, has now become a key area for the biopharmaceutical industry to optimize and address. The industry must shift from a pure cost-reduction model to focus on innovation-driven efficiency. The main question to be answered by the industry is: 'How do I get more done without increasing resources?'

The Merging eClinical Ecosystem

Accenture finds that clinical trials are supported by a variety of technologies that capture, process, and share data. CTMS is one of the many components alongside different technologies in the clinical development infrastructure, such as clinical data management systems (CDMS), electronic data capture (EDC), electronic patient reported outcome devices (ePRO), interactive voice response (IVR), laboratory processing, statistics and programming, and various submission components.

These elements form the interconnected environment that can be identified as the eClinical ecosystem. It is an environment in which high-quality data is of the essence. At its end, it must support the analysis required to provide a safe drug for the patient population but, through the clinical development process, it must also help the industry in maximizing investment by driving the highest efficiency process possible.

By having an ecosystem in which information can flow, data can be taken and used not only for analysis but also for management to comprehend the trial progress, as well as trial-specific predicted events. In essence, within the eClinical framework the technology components need to enable two fundamental processes:

1. data handling (data management, data analysis and reporting, data analytics, and data mining); and
2. trial management (planning, execution, management, and decision making).

Accenture notes that advances in data warehousing and data analytics technology are enabling the evolution of data hubs that can support data handling and the creation of operational data marts that better support trial decision making. With these capabilities in place, the two focal points—one data focused and one execution focused—can come together and CTMS can become the operational 'heart' of the clinical trial process. The direction of future approaches will determine just how much CTMS will gain in strength as it is established as the master system within the eClinical infrastructure.

1. Baum A, et al., Pharmaceuticals: Exit research and create value, Morgan Stanley Research Report, January 2010.
2. NMEs Approved by CDER. Available at: www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM247465.pdf (accessed June 2011).
3. Pharmaceutical Industry Profile 2010. Available at: www.phrma.org/sites/default/files/159/profile_2010_final.pdf (accessed June 2011).
4. DiMasi et al, The price of innovation: new estimates of drug development costs, *J Health Econ*, 2003;22(2):151–85.

© TOUCH BRIEFINGS 2011

The future position of CTMS in the market will be dictated by how these technologies leverage key opportunities created by changes in the technology landscape, as well as changes in the way the industry executes clinical trials. The main factors that will contribute to the future positioning of CTMS include:

- capitalizing on analytics
- improving and driving the workflow
- consolidating master data; and
- becoming the central, integrated management solution.

The Impact of Analytics on CTMS Functionality

Considerable value can be added to optimize decision-making and making the process more strategic by implementing data analytics tools. CTMS becomes more than just a project or trial management environment when clinical and performance data can be used to help predict the success of a trial, understand the feasibility of the trial design, or even change the parameters of a protocol or study design. The ultimate result is a more successful and efficient clinical trial. Cost reductions can be achieved by modifying various parameters including the number of patients recruited in a trial, the number of trials executed, and the number of sites used—all of which can drive a cost reduction of ~30 % in trial expenditures.

Analytics will prove even more valuable for clinical trial execution where the value of external data, including electronic health records (EHRs), and payer and other pharmaco-economic data, can contribute to the protocol design and feasibility analysis of a trial. In analyzing the data from previous trials, these findings could be applied to make decisions regarding future trials, thus increasing the chances of success.

To meet future requirements, as described above, CTMS needs to take advantage of all existing data, not just CTMS data. The insights deduced can assist in making decisions about clinical trials before they commence. This is considered predictive analytics or predictive feasibility analytics.

Information about a clinical trial, such as: the type of trial; the therapeutic area; country of conduct; patient numbers; and details of what the exclusion/inclusion criteria are, can be determined by advanced CTMS capable of mining data from previous trials to determine the current trial feasibility and the chances of meeting overall deadlines. At the fundamental level, a CTMS needs to evolve to a point where it is not just the execution center but also a core to leverage data to perform predictive analysis and improve the overall design of the trials from the start.

Lastly, CTMS can become a central hub that enables adaptive trials. Providing the dashboards required to make the rapid decisions that shape and guide the path of adaptive trials design requires access to key data from clinical systems, rapid analytics, effective visualization, and future modeling of the expected changes. This capability is currently being managed through ad hoc tools, and a packaged, consistent solution would allow the adaptive trial model to be scaled appropriately within an individual company.

The Role of CTMS in Improving Workflow

The strength of CTMS lies in addressing shortfalls in the operational side of clinical research. This can include site performance tracking and management, resource and supply chain management, and regulatory document management. It can be argued that non-clinical workflow inefficiencies have as much impact on the cost of clinical research as working with paper case-report forms (CRFs).

CTMS can excel in its ability to calculate performance metrics and subsequently support rapid business decisions. Performance data can be utilized to aid in constructing proposals that offer the sponsor a truer picture of what can be achieved within agreed timescales. If an organization can observe its performance in certain tasks—or how effectively it carries out tasks in a certain location—this data can be harnessed to optimize workflow, thereby creating a predictive, rather than a reactive, system. This use of data can have positive implications for optimizing decision-making processes and, ultimately, benefiting the contract research organization (CRO)/sponsor relationship.

One area that can be harmonized—and is on the way to being so within biopharmaceutical—is the definition of models in which the execution or engagement of the information provided by a site is being standardized. By incorporating a global registration of sites across clients and sponsors the model would be vastly simplified. By simplifying the clinical trial model a site should be able to perform trials more easily as opposed to going through the significant effort seen currently.

To achieve the best levels of performance, CTMS will also need to play an increasingly significant part in driving high-performance clinical trial execution. The central position of the CTMS in the overall information cycle is further complicated by the wide range of stakeholders involved in CTMS implementation. Although it can be noted that study management must drive the implementation, the study management group must collect and consider input from other groups such as data management, finance, and contract management. CTMS that is built on open architecture and facilitates data exchange with third-party applications can bring significant cost savings to biopharmaceutical companies and CROs.

Consolidating Master Data

Most biopharmaceutical companies utilizing CTMS are looking at master data management opportunities, where key, non-transactional data, such as investigator names and addresses that are often recorded in multiple places, are handled once and unnecessary repetition is therefore avoided. Master data management allows for key data to be stored in a higher quality format across multiple systems while a centrally-managed approach allows for significantly better control over the key data.

The ability to handle large quantities of changing core data will be a vital element to optimizing the clinical trial process. Master data management strategies can ensure that key data are consistent, definitive, and of high quality. The benefits of a master data management solution can be realized by utilizing technology to bring all of the key data together in an integrated fashion.

Currently, data is now coming directly from source systems and standardized, which vastly improves the data quality. In the past, key data, such as an investigator's professional details, were entered manually and biopharmaceutical companies could have several different variations of an investigator's name recorded even though they were the same person. Its central position in data flow makes CTMS ideally suited to drive master data management processes and utilize the master data to support quicker decision-making.

A Master System in the eClinical Framework

Evolution requires modifications to adapt to a changing environment. In the clinical trials technology ecosystem, key changes include the number of technologies in play by sponsors, CROs, vendors, and sites (even within a single study), and the demand to work quicker and more efficiently. This demand has been responsible for accelerating CTMS tools to the next level of performance, use, and functionality. No one could argue that managing research programs and studies with configurable off-the-shelf software is not a challenge. Those involved in running a trial include the sponsor, contract research organizations (CROs), ethics committees, local and central laboratories, and the investigative sites and patients themselves. Because each of these stakeholders have their own needs and specific tasks to be recorded by the different eClinical components (ePRO, EDC, IVR, etc.), the CTMS is in a position to become a central system to coordinate data and workflows and present dashboards for relevant stakeholders. By its current definition CTMS is not yet ready to be a master system but, if it evolves and integrates with other parts of the eClinical continuum, it could well make a compelling case to be just that in the future.

To achieve this scenario Accenture asserts that several changes need to occur. Trial execution has to be standardized and not significantly customizable or configurable. The CTMS is a strong contender to become the central master system to coordinate meaningful information within the clinical trial progress. However, whether it will fulfill this role is still up for debate. From a technology perspective, the creation or consolidation of operational systems and a data warehouse that can provide clinical trial management capabilities is another possibility. This scenario is pertinent because a CTMS is not a data warehouse, thus a warehouse is still required for the integration and management of data. Accordingly, the existence of a data warehouse that incorporates CTMS capabilities may be a more realistic central master system.

The Value of a Data Hub

Accenture notes that the biopharmaceutical industry is moving away from the concept of a data management system being the sole place for data to reside and toward a data warehousing or data hub view. Current industry thinking also dictates that if data can be efficiently mined for analysis and reporting it does not really matter what type of on-premise system one has. Data warehousing and the ability to have message-driven technology, in which messages are not constantly replicated, should theoretically be very valuable in the clinical trial space.

The clinical trial process is highly complex and often data are simply moved from one system to another. There is also the added complication of constantly evolving data forms and models, with the potential for new types of data and new usage. While data standards exist, challenges still abound, especially as standards are yet to fully mature and be universally accepted. Therefore, data warehousing and the integration of data into one environment could enable data accessibility across studies and various clinical trial programs. This would allow companies to create complex data models that help to inform best practices that improved clinical trial execution, from determining how best to design a trial to possibly predicting the likelihood that a compound will not work.

Notably a data warehouse is, first and foremost, a working middle ground where a significant number of incompatible hardware, software, and operational systems, accumulated over many decades, are linked to a group of platforms utilized by the end user. To realize real benefit from data warehousing, it will be necessary to define the appropriate data model for the data warehouse.

By applying a common data model to all data regardless of its origins, Accenture asserts that data become easier to analyze and interpret. A data warehouse then becomes a driver toward standardization and becomes a bridge for pharmaceutical companies to exchange data with CROs, partners, and regulatory agencies. As soon as datasets are stored in an agreed format it becomes possible to transfer them to a data warehouse in a standard that is acceptable by regulatory authorities. It should also be noted that, in the data warehouse space, metadata management also poses a significant challenge. Metadata will be a critical enabler of data warehousing functionality, and will help drive the push for data transparency. Metadata, and particularly automated metadata, makes data analysis a much easier task. Therefore, deciding early on, which metadata to utilize, will be critical. Near-perfect metadata content will be required to drive data integration, as imperfect metadata will cause the data integration tasks to fail. A centralized approach to metadata management is preferred as it allows for significantly better control over the metadata.

One of the biggest challenges for a CTMS is to ensure the relocation and maintenance of up-to-date, quality data. Larger biopharmaceutical companies with vast amounts of legacy data have found this to be a particular problem. The overall aim is to maximize the value of data—a task made infinitely easier when data are transparent, reusable, and readily integrated. CTMS is able to generate better quality data if transparency and reusability are factored in. In this scenario, aiding automation of data integration through a master source of metadata that is definitive, consistent, and authoritative will allow sponsors to make better and faster decisions about the status of a clinical development program.

Future CTSM Challenges

Today most CTMS solutions are customizable to a large degree and observations have indicated that this is not a completely standardized area. Common requirements include project management, budgeting, financials, patient management, investigator management, ethical approvals, compliance, and integration with other clinical systems. One impending challenge questions the task of balancing the need to customize/configure with the need to introduce a degree of standardization between systems, software, and sites. The biopharmaceutical industry needs to start making choices about what is required to create the best possible tools. As these tools evolve, companies will eventually work with the vendor population to develop the next generation of systems so that the need to customize is negated. By leveraging the vendor population to push for changes covered by the license, the drive may well be the start of new and innovative releases of industry utilities. Increasingly, software and service models are emerging in which a vendor or software company hosts and provides access to trial management technologies.

Another challenge is the need to manage more complex and adaptive trials. Adaptive trials have the potential to improve clinical drug development; however, they will also introduce more complexities.

With the concepts involved in adaptive trial design, tracking the status of the study against a planned objective would be difficult for CTMS if planned objectives changed on a regular and frequent basis.

Lastly, Accenture research indicates that budgets for information technology continue to shrink and the opportunity to expand the capabilities of CTMS technologies to suit individual company needs are becoming less. Therefore, packaged solutions that are configurable will need to deliver the expected value with minimal cost for implementation and long-term support. If the total cost of ownership of CTMS systems does not significantly decrease, the business case for CTMS expansion will become weaker, threatening its long-term need and survival. Over the past two years there has been a slowdown in the number of new CTMS implementations, which may signal the lower value assigned to its capabilities in comparison with the costs required to implement them.

Concluding Remarks

The competitive nature of the current marketplace is driving the biopharmaceutical industry to search for more-effective ways of decreasing drug development times and increasing productivity. Accenture believes that CTMS technology has stimulated new demands for enhancement, configurability, and intelligent features.

The call to further develop clinical efficiencies and expedite study times continues to gather pace, motivating industry sponsors to find an eClinical environment that enables adaptive trial design, solid data management, real-time data visibility, reporting and analysis, and global trial management. By adopting and embedding CTMS technology into the eClinical infrastructure these technologies will play a greater part in drug research and development—becoming more prominent as clinical trials become larger and more complex. In a globalized and multi-faceted environment, technology has to respond accordingly evolving to a point where data is collected in the most passive manner possible, exchanging data seamlessly between applications and services and requiring only minimal data entry from anyone. It is not enough to purchase and install the system. To maximize its value and return on investment an organization should be innovative and progressive, looking to take advantage of all of its systems to support the business. From an architectural perspective, the optimal environment for trial conduct success will be the vendor that offers the most cost-effective integrated solution to a data-centric market. ■