Clinical trials management systems - a review

A fully functional clinical trials management system (CTMS) can help ensure that clinical activities are carried out in line with time and cost schedules.

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While the pharmaceutical industry has been experiencing a period of unprecedented change, the IT industry has been enjoying a parallel boom in the development of new techniques, with significant implications for the management of clinical trials. New ways of capturing data, innovations in Internet deployment and a recognition of electronic records by regulatory bodies are transforming the trial management process.

What is a CTMS?

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A CTMS package is an integrated suite of applications, sharing a common database, designed to help manage clinical activities at different levels - from project, down through a trial, to individual countries running the trial, sites/investigators and patients. For the multinational company, a CTMS package provides a network linking medical departments and operating companies throughout the world, providing a common access to information. It is the key business system for clinical research.

At each level, from project to patient, a CTMS provides options to facilitate the planning and tracking of relevant clinical activities. These might include:

- Planning and tracking of events, approvals, enrolment, documents, monitoring visits, patient visits, case report forms (CRFs) and so on,
- Budgeting, projecting and tracking costs,
- Forecasting and tracking clinical supplies.

Typically, each company will configure the CTMS to manage information appropriate to its own processes. The organisational structure will also be mapped onto the system to define access rights. So, for example, the system may be configured so that a central study manager maintains an enrolment plan for a trial as a whole, while local country plans are maintained by appropriate managers in the operating companies worldwide and actual recruitment for individual sites is recorded by responsible clinical research associates (CRAs). The CTMS automatically pulls all this information together by consolidating information between the levels. The study manager, looking at the overall trial level, can then
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see not just the general enrolment plan, but also the consolidated country level plans and a rolled-up total of up-to-date recruitment figures from all sites.

In the same way, the CTMS can use the entry of information to trigger an update of key dates automatically. For instance, as recruitment information is entered, the CTMS can set dates for ‘first patient-first visit’ within an individual site or at higher levels as appropriate. The CTMS then facilitates automatic comparison of actual dates with the overall plan, plus the facility to re-schedule automatically if needed. In this way, the CTMS provides high visibility of progress at all levels, with early warnings of potential problems and delays. With more than 75 per cent of the time taken to achieve a product licence dedicated to clinical trials, a CTMS has a key role to play in ensuring that trials progress to plan.

A CTMS also helps streamline the effort and cost associated with managing clinical trials. In general, the CTMS provides clinical staff with a framework for managing trials with benefits such as automatic roll-up of information, consolidation and distribution of information worldwide, and the elimination of transcription from paper systems. A particular example is the support provided by a CTMS for CRAs during monitoring visits. By downloading information to CRAs in the field, they can be provided with a prompt for the monitoring activity required. Once the CRAs have entered monitoring details, a trip report can be produced automatically, and updated information can then be uploaded to the main system.

In summary then, a fully functional CTMS can help ensure that clinical activities are carried out in line with time- and cost-schedules, with minimal resource implications.

The Phase I environment

In a Phase I environment, a CTMS shares many of the requirements of Phases II to IV, but also has to accommodate the specialist requirements of managing Phase I units. Phase I is epitomised by short time-scales and high levels of activity. It is this intensity of clinical operations that presents a special challenge - Phase I is all about planning, scheduling and efficient data collection. A Phase I CTMS has to focus on managing the unit and the logistics of taking and handling samples. Extended CTMS solutions are available to accommodate these special needs.

When is it not a CTMS?

We have found some confusion surrounding the overlap between CTM systems and data management systems, electronic data collection (EDC) systems, enterprise project management (EPM) systems and ‘financials’ systems.

Essentially, data management and EDC systems deal with the collection and storage of clinical data, rather than the management of the clinical process.
EDCs are often referred to as having ‘trial management capability’ - but this tends to be restricted to the site level. More usually, data management systems and EDCs act as sources of information for populating a CTMS with recruitment figures and so on.

Enterprise project management systems are generic project management solutions, often used to manage overall projects from discovery to final submission. Such systems tend to hold information at a higher level than a CTMS, and are not structured to support the processes and levels within a clinical organisation. The two systems can, however, work together; it may be that summary-planned dates for clinical activities held in an EPM can be loaded into a CTMS and then, as detailed ‘actual’ dates are captured in the CTMS, summary dates can then be loaded back into the EPM.

‘Financials’ systems also tend to hold information at a higher level than a CTMS. Again, there are overlaps but typically the functionality is complementary. A CTMS, for example, can reduce the effort required to track investigator payments, with the system automatically knowing when payments are due, based on payment criteria being met - for example, a particular recruitment level; once authorised, payment requests can then be passed to financial ledger systems to generate the payment.

Systems integration

Clearly, there is considerable overlap between CTMS and other systems, and it makes sense for a high degree of integration between these and other in-house systems. At its simplest, integration means that information can be passed electronically between systems, making it more rapidly available where needed, whilst avoiding transcription errors. Transfer of recruitment updates, event dates and payment requests, as mentioned above, are typical examples of data that can be passed electronically between systems.

In the past, this would have been achieved by writing direct links between applications, or by building intermediate databases mirroring data in core applications. Even if vendors make the relevant information about the ‘internals’ of their application available, this integration is still a time-consuming and complex process, and intermediate databases often get out of sync with the databases they are mirroring. Furthermore, new releases of software from external vendors always have to be checked to ensure continued integrity of the links, creating - in short - a nightmare.

An infinitely simpler approach has emerged; it goes by the inelegant name of an Application Program Interface (API) - something that should be provided by CTMS and other systems suppliers. Essentially, an API in this context is a

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Clearly, there is considerable overlap between CTMS and other systems, and it makes sense for a high degree of integration between these and other in-house systems. A software routine that updates the CTMS database with a particular type of data. For example, an API might deal with updating a patient visit. When details of a visit are received from the external system, the API could:

- be used to validate the data against the CTMS database - for example, is it for an existing patient?
- carry out all the necessary integrity checking and update the database - for example, check whether the visit is the first for that patient and, if so, update an associated status and event date for that investigator site, or check whether this is the first patient-visit in that country, or in the trial as a whole, and update any associated statuses and events.

In other words, the API contains all the integral processing that would be carried out if a visit had been entered manually. With access to APIs, the question is not How do I develop an interface for each external system? but How do I extract data from each system for use with the supplied APIs? In general, extracting data is a far easier option.

Reporting

A modern CTMS will support sophisticated reporting tools that can extract information in both standard and ad-hoc ways, enabling users to report on any of the stored information. With a mixture of paper reports, web-based reports and mail-merges, there is now a rich variety of formats for presenting management information.

On the one hand, a CTMS can provide a current picture of clinical activity, summarised at any level from project through to patient; on the other hand, the CTMS database contains a history of clinical activity - providing an invaluable aid to looking at past performance and generating metrics.

The role of the Internet

Whilst the basic demand for the functionality of a CTMS will not disappear, the e-clinical revolution means that CTMS technology must adapt to take best advantage of the Internet.

The Internet is really just a Wide Area Network (WAN) that supports low cost electronic communications around the globe. Recent improvements in security are allowing companies to operate their own private network using the Internet as a low cost infrastructure. The Internet means simpler and more widespread access to CTMS through web browsers; devolution of CTMS access to a wider community of more occasional users becomes a reality. With the trend towards more e-systems, there are extra opportunities for integration with other systems.

In Figure 3, access from web browsers allow simple update of recruitment worldwide.
providing faster and more accurate management information at all levels around the globe.

Developments in the Internet are also making it possible to deploy computer applications in new ways. We are beginning to see a return to the concept of service bureaux with the Internet being used as the delivery mechanism - 'Hosted Services' provided by an Application Services Provider (ASP). The bottom line is that a fully functional CTMS can now become accessible to organisations that might previously have felt excluded on the basis of cost, initial overheads or difficulty in justifying a relatively low usage.

Using the Internet to link users - via their PC workstations - to an on-line bureau eliminates the need for a dedicated network, resulting in significant hardware savings. As the application is provided on a bureau basis, there is no requirement for in-house skills in software such as Oracle - skills that are not easy to find and can be expensive to retain. Software maintenance, implementing upgrades and so on, are also simplified because maintenance becomes the responsibility of the service provider on a centralised basis.

The ASP model also opens up possibilities for new pricing mechanisms, such as monthly software rental or even a fee-per-trial. This may be particularly attractive in the CRO environment, where costs can be recharged to the client, without the need for a significant up-front investment.

Conclusion

Less than five years ago, CTMS packages were seen as immature systems, with many companies taking the decision to develop in-house solutions. Today, CTMS packages are well-established - providing rich functionality and taking advantage of the latest technological innovations. CTMS packages have finally come of age.

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