Integrated IT Systems and the Challenge of Globalisation

Fast-moving information is key if mid-sized CROs are to keep up with their larger competitors, and the best way to do this is with an integrated clinical trial management system

Lars Behrend and Michael Sigmund at SSS International Clinical Research

Information flow is a key factor in the project management of global clinical projects. Project managers (PMs) of international clinical trials rely on timely and properly consolidated information for successful navigation of projects. In an outsourcing concept with many subcontractors, assuring the appropriate management of interfaces can be particularly challenging. The bigger the study, the higher the number of sources delivering content that PMs have to pay attention to. Sponsors using an outsourcing strategy have to address the question of how to handle these different sources of information and interfaces. This can be especially challenging if vendors and specialists are not part of one organisation, but are using different IT and reporting systems. Tethering all participating bodies within a project to one central IT system helps to unify and pool documentation, reporting, and information flow. In the field of clinical research, clinical trial management systems (CTMSs) offer this type of centralised IT system for the integration of processes. These CTMSs open up new possibilities for mid-sized CROs as even big international projects can be delivered as soon as sub-contractors are linked worldwide via a CTMS.

Increase in Globalisation of Clinical Research

Clinical research has become even more global in recent years. This is for several reasons; the increasing wealth of populations and the improvements in health systems have made emerging countries more attractive as pharmaceutical markets. At the same time, the widespread use of ICH-GCP guidelines also helped to implement worldwide quality standards that are a prerequisite for multinational clinical trials to gain a reputation and recognition (1). All of this has led to more trials being conducted outside of the classical 'trial countries', such as the US, Japan, and countries in Western Europe (2-3).

Oversight is the Central Task of Sponsors in Outsourcing Models

With increasing globalisation in the clinical research sector, trials have

become larger and more complex. Even in large pharma companies, this has resulted in an overload of internal capacities. As a result, the previous model of having a large number of in-house professionals dedicated to clinical studies with responsibilities in protocol conception, execution, and oversight has transformed into a model involving both internal and external capacities (1). Today, central tasks of clinical trial activity, such as monitoring, are mostly covered by CROs, whereas sponsors remain responsible for oversight and control.

In the business model of biotechnology companies, which are often financed by venture capital, low fixed costs have always been key. Outsourcing a broad portfolio of services can keep fixed costs low, thereby allowing biotech companies to be more flexible. In recent years, the industry has even developed the model of 'virtual biotech', where a very small internal team organises the complete developing pipeline by using external vendors (4). In this model, biotechs have to outsource in a way that allows easy oversight and quick response to non-compliance and unwanted developments. This is even more essential for biotechs than for pharma companies.

The Bigger the Study, the Bigger the CRO?

Once the decision has been made to source out, there is always the question of who to work with: one global or several smaller, more specialised CROs? Sponsors tend to decide to work with global organisations all the more if the trial involves many countries and is rather complex. Although there is an awareness that smaller CROs sometimes offer more individual and customer-focused services, Big Pharma companies are used to working with global CROs (5-6). However, it is a fact that the high turnover of staff in big CROs results in low team consistency over the course of a trial. When working with global CROs, smaller sponsors also have to fear that they "get much less attention than the large pharmas where they have preferred arrangements with and the bulk of the revenue is generated in those organisations", noted Marty Driscoll, CEO of Spring Bank Pharmaceuticals, Inc. (7). However, even small sponsors that want to perform multinational trials often decide on big CROs. Indeed, big CROs have broad capacities pooled in a single organisation. As reports and updates originate from one source, contracting one company for all services seems much simpler, promising better control and oversight.

'One-Stop Shopping' When Outsourcing

Just like in other industries, internal resources in the pharma industry were shut down or drastically reduced over recent years. Consequently, teams in clinical operations sometimes struggle to even fulfil the central function of a sponsor, i.e., keeping control and oversight. Nowadays, most sponsors contract only one CRO that is in charge of the whole study. This 'one-stop shopping' reduces interfaces and information flow to one partner who is responsible for all sub-tasks and all geographic regions of the study. Big CROs can cover many of these subtasks within their own organisation. The interfaces between investigational medicinal product (IMP) management, safety, monitoring or medical monitoring, to name only a few, must still be synchronised.

In mid-sized CROs, these interfaces are frequently planned outside of the organisation as more subcontractors are needed to cover all aspects of a global project. Even though the contractual partner is responsible for all sub-tasks, sponsors often lack confidence in mid-sized CROs. The main concern is that the interfaces located outside of the CRO cannot be organised and synchronised as efficiently as if they were part of the company structure.

Cherry-Picking Complicates the Management Process

Contracting smaller service partners in a cherry-picking approach bears the disadvantage that any of these CROs may have their own IT systems with different reporting tools. The experience of most sponsor PMs is that vendors deliver reports with different topicality, different information depth, and perhaps even different definitions of key performance indicators. Contextual and timely consolidation of different reports is time-consuming and involves a high risk of failure. Differential reporting standards also make it hard for a PM to report to upper management. Here, a central IT system used by all sub-contractors can help to standardise information. Keeping oversight and making the right decisions depends on easily understandable and integrated information. An outsourcing approach, where specialised CROs being the best in their region or offering specific services are contracted, can only be successful if the sponsor has the tools to integrate and harmonise the study information. As outlined in **Figure 1**, a CTMS can be the central source of information and reporting, setting standards by defining which information is crucial, the topicality content has to meet, and depth of information to be provided.

Ideally, the interfaces of the CTMS can be adjusted individually to the IT systems of the different providers, thereby, the desired data are automatically transferred to, and displayed in, dashboards of the central CTMS and releasing providers from the task of manually submitting these data to the CTMS. The CTMS additionally simplifies management functions by implementing processes and business logics that are capable of being automated (e.g., a specific trigger generates queries or messages within the team).

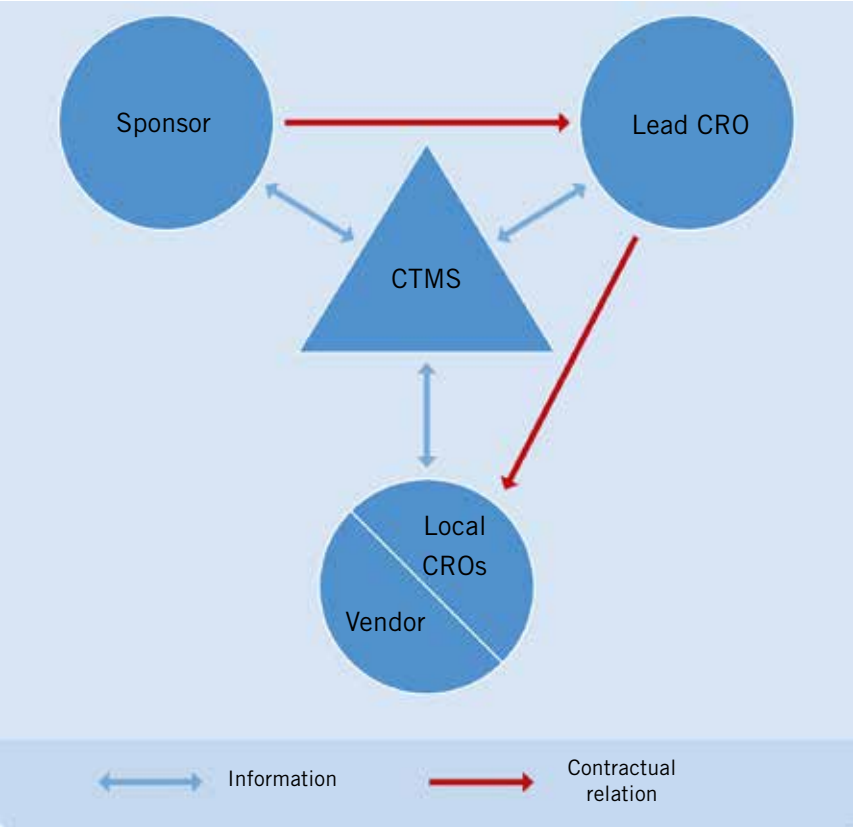

Figure 1: The authors make use of a CTMS as central working and reporting tool for all study participants. Handling large multinational trials with a centralised CTMS for documentation and information flow allows sponsors to keep track of all aspects of the trial, despite most of the information being generated by sub-contractor

CTMS Has Become Standard

It has been a decade since the early days of CTMS, and now it is standard in the field of clinical research. A growing number of CTMS software has been launched by different companies in recent years. These systems have a host of functionalities central to clinical trial management, e.g., assisting with keeping track, creating reports, and identifying time-critical paths. Key features include a customisable web page, sophisticated access control mechanisms, and the possibility to connect to other systems. Most of these commercial off-the-shelf (COTS) systems are based on software as a service, and are therefore easy to use and highly convenient. On the other hand, COTS offer only limited flexibility when applications require customisation in response to specific customer needs. Clinical projects often differ in terms of geographic location, distribution of tasks between different stakeholders, or object of study (i.e., medical device or IMP). Limited adaptability could therefore be a disadvantage for the user. Additionally, COTS are cost-intensive and CROs may face problems transferring the costs to the sponsor of a study.

Different Options for Implementation of CTMS

For most mid-sized companies, COTS systems are the first choice when implementing a CTMS, as programming of a newly developed CTMS is usually not a feasible option. Indeed, developing source code from scratch requires a dedicated team of programmers and substantial funds and time resources. The development of a customised CTMS solution based on a low-code platform could provide an alternative. Low-code platforms significantly reduce the development time needed, since

most levels of technical skills can access and use them as the biggest proportion of programming is done automatically. The standardised toolkit used in these systems facilitates consistent quality and usability for programmers and users alike. Elements can be drag-and-dropped into spaces on the webpage and configured to satisfy all needs of the company and the customer. Configuration includes aspects such as appearance, visibility, and function. Data for these systems are usually stored securely in the background using modern on-premise technologies or cloud solutions. Commonly used products for the background data model are Microsoft SQL Server, Oracle, or MySQL. These software products all handle data in a relational model optimised for a low-code approach. This provides the company with the best ratio between complexity, adaptability, and performance.

CTMS Help Small Teams to Face Global Challenges

When sponsors outsource a larger part of a clinical research programme, they always buy into the operational competence of a CRO as well. Many mid-sized CROs that have been on the market for a long time have a great deal of knowledge in operational questions. Nevertheless, it is pivotal for the CRO to establish a standard of practice when most of the tasks have been outsourced to a variety of subcontractors. For many smaller CROs, this often represents an obstacle as their systems are not designed to handle diverse study tasks or international study teams. Here, a self-developed CTMS does not only allow to display internal processes in a standardised way, but also projects these standards onto external tasks of sub-contractors. A brilliant example are cross-team-workflows: a team starts a workflow, which is then delegated to other defined user groups for completion. After these groups have fulfilled their respective tasks, they can send the workflow directly to the sponsor for approval. Such cross-team-workflows reflecting business logics are of invaluable worth when the assignment concerns large multinational projects or when the CRO has to handle diverse tasks on behalf of the sponsor. Making use of automated routines is even more important for the management of projects with interacting teams from different executing companies.

Taken together, once a standard procedure for the conduct of clinical projects has been defined, a flexible CTMS offers the possibility to map a wide range of internal processes leading to harmonisation of work routines. It also offers the intriguing chance to connect to teams outside of the company, thereby enabling oversight and navigation of the project. In a landscape of growing complexity and globalisation, this standardisation across company borders allows even mid-sized CROs to manage large scale projects.

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Lars Behrend, PhD, is currently Chief Operating Officer (COO) at **SSS International Clinical Research**. He studied Biology in Hamburg, and after receiving his PhD in Molecular Oncology in 2001, Lars worked another four years in the oncology field at the Interdisciplinary Center for Clinical Research in Ulm, Germany. He has published various articles in peer-reviewed journals. After leaving university he started two venture capital-financed companies and a consulting firm in the life science and cleantech field. In 2017, he joined the management board of SSS. For 16 years in Chief Executive Officer and COO positions, his main focus is in strategic positioning and commercialisation of products and services.

lars.behrend@cro-sss.de

Michael Sigmund, DVM, is Chief Executive Officer of **SSS International Clinical Research**, which provides CRO services to the pharma and biotech industries. Michael has more than 30 years of experience in the field of clinical research. After studying Veterinary Medicine, he did research in the field of virology and received his DVM in 1988 from the University of Munich, Germany. He then joined the pharma industry and held several positions within biotech and contract research companies. Michael has ample experience in setting up and running clinical trials. His main interest lies in streamlining information concerning clinical trials to allow easy and effective access to relevant status information for all parties involved. Michael helped significantly to develop SSS's professional web-based CTMS called accSIS.

michael.sigmund@cro-sss.de