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Ongoing Trends and Strategies to Fine-tune the CRO/Sponsor Partnership - Perspectives from Statistical Programming

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ABSTRACT

Sponsor and Contract Research Organization (CRO) partnerships are becoming more frequent, and critical in the management and handling of data from clinical trials. In this paper, we describe various types of these interactions, factors that shape and govern these interactions, and pros and cons of each type. Additionally, we highlight how multiple factors on both sides determine the magnitude, length, and scope of the relationships. Outsourcing relationships range from short-term transactions to fully integrated partnerships. While partnerships occur in a variety of clinical trial processes, here we focus on the business processes surrounding the needs of clinical and statistical programming. In this paper, we propose effective strategies for optimizing conditions to foster a fully integrated long-term Sponsor-CRO partnership that benefits both sides, and enables high quality clinical submissions.

INTRODUCTION

Good Clinical Practice (GCP), an international quality standard set forth by the International Conference of Harmonization (ICH), clarifies that a CRO is a person or an organization contracted by the firm that owns a drug development program for carrying out some of all of the steps involved in the drug development process. Clinical trials are a vital part of drug development, allowing the sponsor to evaluate the safety and efficacy of new therapies before they are approved for use by patients. Conducting clinical trials is a complex and time-consuming process, involving a spectrum of activities from patient recruitment to data analysis, some of which may be outsourced to external organizations by the pharmaceutical companies. Outsourcing can be broadly defined as the business practice of hiring a party outside a company to perform services or create goods that were traditionally performed in-house by the sponsor's own employees. The biotech or biopharma companies owning the drug development pipeline are often referred as sponsors because they completely own and oversee the outsourced activities contracted to the CROs.

Currently for many pharmaceutical firms, outsourcing all of their clinical trial activities to CROs offers many benefits, and hence becomes a popular option**.** By virtue of their experience from handling multiple clients and global regulatory agencies, CROs can also help companies navigate complex regulatory requirements. Thus, outsourcing to CROs can help pharmaceutical companies reduce costs, accelerate timelines and access specialized expertise and resources, thereby increasing the chances of success for drug development. For example, small size biotech/biopharma firms at the beginning of their growth cannot afford to have their own resources devoted to late-stage clinical trials, and hence outsource their late-stage development to CROs. In addition, large biopharma firms also outsource to CROs so they can focus their resources on early drug development programs and build stronger pipelines. CROs need revenue from sponsors to survive in the industry, and sponsors need complete submission packages generated by CROs in a timely manner and in compliance with all applicable regulatory submission requirements. Hence this is a win-win situation for both parties.

Regardless of the nature, duration and outcome of the clinical trial contract activities being conducted by the CRO, sponsors are ultimately responsible for the initiation, management, and financial aspects of the clinical trial. Throughout a trial, the sponsor is also ultimately responsible for implementing and maintaining quality control via written SOPs and guidelines, and ensuring that the clinical trial is conducted and the data are generated and subsequently processed in compliance with the protocol, GCP and any other relevant regulatory requirements. CROs in turn must have their own quality control assurance and implementation processes and relevant documents must be maintained properly and ready for audit any time by the sponsor and regulatory authorities.

We broadly define this interaction between sponsors and CROs as a partnership since both parties enter into an agreement for conducting and completing various stages of the clinical trials, and thus this interaction essentially represents a symbiotic relationship. Duration of the partnership can be short-term, long-term strategic or transactional. Partnerships between CROs and sponsors are no longer a new strategy, and continue to evolve and mature as both parties constantly learn from each other.

While the partnership between CROs and sponsors reflects the business nature and benefits for each, the nature of the partnership affects its stability and thus the length of the employment of the existing programmers. In this paper, we offer insights on the various types of sponsor/CRO partnerships that currently exist in the industry. Additionally, we identify areas within these interactions that can be further fine-tuned so that both parties can benefit each other. In the end, readers can visualize which model of partnership can be helpful from the point of sustainability of the business model and career prospects for the programmers.

BUSINESS MODELS IN CRO/SPONSOR PARTNERSHIPS

Having established the business needs for both sponsors and CROs, the interactions between these two parties are very intricate, knowledge-based and involve many risk factors. In order to fully appreciate the nature of their relationships, it is necessary to understand the models of interaction that currently exist. These models can be broadly divided into three categories: (1) The first and traditional one is the CRO with in-house capabilities. In this model, the CRO has its own programming platform and facilities sufficient for carrying out all clinical trial related tasks for any sponsor. (2) In contrast to the first one, the CRO embeds its programmers into the sponsor's platform to carry out the programming tasks required by the sponsors. This Full-Service Provider (FSP) model is becoming increasingly popular as many CROs have adopted this setting. (3) The third and smallest model consists of independent contractors who independently provide programming services to sponsors. From an outsourcing perspective, since the sponsors outsource their programming tasks to an independent contractor who will essentially still be working in the sponsor's platform, he/she can be called a CRO.

CRO WITH IN-HOUSE STATISTICAL PROGRAMMING CAPABILITIES

This model is well-known as it has been around since the concept of outsourcing became popular. In this setting, the CRO wins business contracts for projects from multiple sponsors concurrently, carries out all agreed-on tasks, and sends the deliverables to the sponsors. CRO typically includes programming team comprising of programmers, statisticians and IT-support resources in various levels to handle multiple projects being contracted by various sponsors (clients). Under this model, the CRO's facilities and technical platform are formally audited to ensure that the sponsors can trust sending their data to the CRO for subsequent analysis. Typically sponsors enter into contracts for carrying out programming tasks with a CRO for either a specific duration or a portion of their pipeline. The extent of the contracts is diverse, beginning with carrying out specific steps such as clinical data management (CDM), Study Data Tabulation Model (SDTM) domains, and Analysis Data Model (ADaM) datasets and their Tables, Listings & Figures (TLFs), to covering the entire clinical development process for a sponsor's pipeline. Some of the major CROs harbor established teams for CDM, data integration and standardization including full SDTM-related services, and a Statistical Programming Team handling ADaM datasets and TFLs, in addition to other cross- functional teams. Apart from these cross functional teams, a few CROs have exclusive Data Standards teams that include experts who have been well recognized for their contributions to creating and advocating for global clinical standards.

One of the notable business advantages for the CRO under this model is that the CRO does not rely on opportunities from a single client; any potential restructuring/cost cutting decisions from a single client does not affect the entire in-house programming team of the CRO. Hence it a sustainable revenue model and thereby ensures sustainable business. While these attributes are impressive, this model does pose certain disadvantages to the CROs from a business perspective. Since this model brings in projects from multiples sponsors, CROs cannot afford to have a standardized programming platform for generating ADaM datasets and TLFs because specifications, mock up and formats for the outputs differ from the sponsor to sponsor.

Programmers spend more time in generating programs from the scratch to cater the specific needs specifications, mock up and formats for the outputs for each sponsor. Possibility of recycling of codes/programs is very less likely. Hence this scenario would result into an extended delivery period due to specific requirements from each sponsor. For the programmers working under this CRO's setting, there are certain promising benefits. Under this model, programmers gain opportunities for learning about multiple sponsors in diverse therapeutic areas following different versions of CDISC standards, especially in SDTM and ADaM. Because each sponsor can be in different stages of their adherence to CDISC Standards' versions. Therefore, the programmers get the opportunities to learn wide variety of programming tasks from multiple therapeutic areas and also to harness their practical knowledge on CDISC standards' implementations by handling variety of requests from multiple sponsors in a short time.

This in-house setting also offers certain advantages to the sponsor as well. If a sponsor utilizes the same CRO for multiple services such as CDM, SDTM and ADaM for the same study or related studies under the same investigational product, any potential changes/data issues at the CDM/SDTM level can be communicated well ahead and resolved from the CDM through the completion of ADaM/TLFs. Otherwise, if these services were given to multiple CROs, communication across multiple vendors about the issues and their resolution would cause significant delays. Hence if a sponsor gets its deliverables for its multiple cross functional teams from a same CRO, it will be good the sponsor from point of data management and analysis/outputs.

Despite the advantages that both the CRO and the sponsor can derive out of this model, there are certain disadvantages for the programmers that we need to highlight here. It is very common for a CRO team to work on multiple deliverables from multiple sponsors concurrently and also, there is a high possibility for getting sudden requests from the sponsors to address revisions for any of their recent deliverables or for carrying out additional outputs with an expedited delivery. In this scenario, head count in the CRO teams need to would be increased to address these unscheduled business requests and this decision would require many factors into consideration in order to be cost-effective. CROs may not be able to bring in more programmers for a short duration. Scalability is highly unlikely when the head count is precisely arranged for the deliverables across multiple clients and any further push to the programmers to accommodate additional works concurrently to accomplish aggressive milestones would affect the working ambience, and eventually may result in high level of attrition among the programming staff.

CRO WITH FSPS

CRO WITH FSP – MERE STAFFING

In many instances, the CRO hires programmers and drops them into the sponsor's programming team; hence in this model, the CRO functions as a mere staffing firm. A managing staff from the CRO side oversees this setting with a role that is limited to being a point of contact between the programmers and their CRO. Part of the reason for this setting is that the sponsor prefers to have total control over the programmers' functions, from the task assignment though the monitoring of work progress and completion of deliverables. The sponsor's team may not want to bear the cost for any managerial responsibilities from the CRO side.

From the view point of advantages of this interaction, CRO's benefit is small in comparison with what sponsor gets out of this partnership. The CRO does not have any oversight role over their programmers working on the sponsor's side, and the revenue (usually a flat charge per programmer) is sustainable as long as the programmers are working within the sponsor's team. If the sponsor decides to reduce the number of CRO programmers due to restructuring or performance, then it is CRO's responsibility for deciding on the fate of programmers' employment. On the other hand, the sponsor benefits significantly in this partnership. Due to the transient nature of the partnership, the sponsor team's approach will be to utilize all the talents that programmer bring in to the table and also to ensure that the programmers are getting their tasks constantly without any unused hours and thereby the continued productivity from the CRO's

programmers are ensured. Sponsor does not have to worry about rendering any additional benefits for the contractors. In the case of any restructuring situation or performance-based terminations, the logistics for the sponsors to terminate the contract for the particular CRO's programmers are fairly simple and quick.

Regardless of the benefits/loss that both sponsors and the CRO team experience out of this interaction, what are the benefits, losses and the challenges that programmers face on daily basis? Under this model, the programmers do not receive any additional benefits, other than the opportunity to work with the sponsor's team. In this model, leading and oversight roles remain mostly on the sponsor's side, and CRO programmers are assigned tasks by the sponsor's team. Hence CRO programmers do not generally receive any project lead-role opportunities to interact with cross-functional teams such as statisticians, data management and regulatory groups. Thus, apart from the programming tasks that can potentially sharpen their programming skills, programmers do not have opportunities to gain leadership and project management skills needed for their career growth. Their managers on the CRO side also don't interact with the programmers closely enough to know any of the issues at the data/project levels, or hurdles that the programmers face. Therefore, this kind of management does not provide meaningful technical leadership or solutions to the programmers. Since the CRO has the least level of responsibility over its programmers, any career goal / year-end review discussion does not mean anything to the programmers since everything is decided by the sponsor's team. In this situation, ambitious programmers who are keen on learning multitasking and leadership skills that are essential for moving up the career ladder soon get bored and leave for other roles catering to their career interests.

Despite the contract for a specific period between the sponsor and the CRO, from the programmers' view, the interaction is transient and transactional. From the view of investment in resource development, there is a significant loss for both CRO and the sponsor when skilled programmers leave the job earlier than the contracted period due to these drawbacks. Time and effort invested in training the programmer in the sponsor's platform are wasted, and it is a loss for both the CRO and the sponsor's teams.

CRO WITH FSP – ACTIVITY BASED COSTING (ABC)

This model typically consists of annual contracts between the sponsor and the CRO with the potential to decide on the continuation of the contract based on mutual understanding. In this partnership, the programmers are employed by the CRO as Full Time Employees (FTE) and are dedicated to work exclusively in the sponsor's platform along with sponsor's programming team as commonly noticed in any other FSP models. However, the operational aspects involved here are unique and involved high level of monitoring at the mid-manager level/lead-programmer level on the CRO side. The way this model is functioning can be described as follows: The CRO charges the sponsors based on programming tasks rather than applying a flat charge for a whole study or a compound/indication consisting of multiple protocols. The CRO determines the cost for each task based on the hours required for carrying out the task. The sponsor's programming team provides the scope and specification for the data and outputs, and the CRO team delivers them. Sponsors provide an overview of upcoming needs on at least a quarterly basis and this allows the CRO to line up their programming resources well in advance. Typically, the sponsor releases the work order detailing the types and number of outputs with a request date for delivery, and requests an initial cost estimate from the CRO. The CRO has its own ways of calculating the hours needed for each task. For example, if a table requires a program that needs to be written from scratch or even if an old program requires major changes to address the requirement, it is categorized as unique; if an existing program needs minor changes or addition of a filter to select a sub-population or category, then it is called a repeat; if a mere re-running of programs without adding any changes is needed, then it is called a refresh. Based on the hours needed for each category, the CRO provides a price for each task. The delivery date is usually rigid, and generally allows little room for negotiations.

The CRO derives more financial benefits from the sponsors through this partnership. In most cases, the actual cost of completion exceeds the initial estimates since the sponsors tend to make changes in terms of number, scope and format of the outputs; thus, the scope of the final delivery volume is larger than the initial estimate provided. This is a great benefit for CRO from a revenue perspective. Since the cost of every hour is being monitored, both the sponsor and CRO teams pay close attention to the ways the hours are being used by the programmers. This is a tightly balanced situation where both the CRO and the

sponsor benefit financially. The sponsor team accomplishes the completion of their planned tasks in a short or agreed time in an efficient manner. However, the programmers and the mid-level managers on the CRO team face many challenges here as every hour of their working is tightly monitored by both parties, and do not have opportunities for thinking about their career path or pursuing career development activities such as learning new tools, or writing and presenting papers in professional meetings.

Since every task is being assessed based on the hours needed for completion, generating an initial estimate of the cost and resources requirements for the whole delivery is cumbersome for a lead programmer or technical manager, though a slight deviation at the end is not unusual. For the CRO's managers, closely monitoring the tasks and assessment of revenue for each week, verification of the revenue for the tasks carried out during the previous week, and preparation of consolidated weekly revenue reports across the studies are very cumbersome in nature. In addition, the managers also attend most of the sponsor meetings to negotiate timelines, and provide technical and strategic guidance to the CRO programmers. Concurrently, these managers also attend frequent meetings with their senior management to provide constant updates and also exchange the inputs across the team. If a manager is enthusiastic and wants to provide strategic/technical leadership to their programming team as a subject matter expert, this model may not allow for this approach, since the main focus of their role is to monitor and manage activities that are driven only by revenue.

It is very common for sponsors to make additional requests/changes after both sides have agreed to the work order. Unless the changes are drastic, the sponsor tends to be keen on receiving deliverables based on earlier agreed-on timelines, despite changes proposed by the sponsor's team. Frequent changes in work orders cause crunch situations for programming resources when actual hours exceeded the estimated hours required for a delivery. The CRO generally determines the number of resources for the delivery regardless of fluctuations due to change order requests, and thus increases the work pressure on the programmers. Time required for tracking and documenting the changes suggested by the sponsor team and issue management needs constant monitoring and communication; these steps consume significant number of hours on par with the programming and are exhaustive for the technical/mid-managers of the CRO side.

In sum, both managers and programmers from the CRO side are always tightly engaged in their roles. Focus on programmers' career planning, learning about new standards and industry requirements is less since they are always working on deliverables under very tight timelines. The working conditions are purely profit-driven, and with less consideration for the programmers' career aspirations. In the end, the programmers do not feel any recognition for their hard work. Continued frustration among the programming resources and a toxic work culture leads to high levels of attrition. Continued attrition then will lead to the shrinkage of the programming team and eventually even closure of the team! As a result, the reputation of the team in the programming world will be severely affected. Therefore, operational aspects described under this FSP model is not healthy in the long run for the CRO as well as its programming resources.

CRO WITH FSP – FULLY INTEGRATED MODEL

This is fairly stable FSP setting that can provide many long-term benefits to both CROs and sponsors. The contract between the two organizations stays a number of years, unless something goes wrong on the business side of the sponsor. Under this model, both the CRO and sponsor work in a collaborative manner rather than under vendor/sponsor terms. The sponsor allows the CRO team to bring in its proactiveness and skill sets and enables them to be part of the decision-making processes related to the programming activities for a given study. This model brings a stable business to the CRO. Importantly, programmers gain much more than what CRO gains this partnership.

The greatest benefit for the CRO programmers is that they are able to work on various aspects of programming tasks, and see cross-functional teams work together from the onset of programming activities through the final packages such CSR, interim analysis, and NDA filings. Hence, the CRO programmers get an opportunity to take ownership and responsibility for their programming tasks. On the sponsor side, usually the programming lead or study manager assigns and oversees the activities across a team that consists of both CRO and sponsor programmers. Additionally, since the programmers have an opportunity

to see the complete scope of the planned deliverables, if a programmer wants to learn a variety of tasks such as efficacy data and output generation, complex figures, Define.xml preparation, etc., this model can cater to those interests. Considering the growing popularity due to the advantages that both parties enjoy under this kind of partnership, the extent of benefits is being discussed further with additional insights eventually in separate sections of this paper.

INDEPENDENT CONSULTING STATISTICAL PROGRAMMERS

Statistical programmers who are not employed formally by a CRO or sponsor, but enter into a contract to carry out the tasks under certain specific terms by an organization are called independent contractor programmers. They are self-employed. The organizations that utilize their skills and services usually do not provide any benefits such as medical insurances, paid vacation, pension, etc. that are normally given to their full-time employees. From the perspectives of outsourcing practices and guidelines, these independent contractors are acting as CROs since they carry out tasks that are outsourced to them by the sponsors.

Generally, the partnership between an independent contractor and the sponsor is very transactional, without any long-term planning. Any time if the sponsor feels that the contractor is no longer required, the sponsor can immediately end the contract. Hence the interaction is purely task/project based, and the contractors are mostly paid on an hourly basis. Usually those with extensive knowledge of programming tools and experienced with complex table and figure generation take this kind of role. The reward factor in this interaction is money. These programmers work under many kinds of models, such as directly embedded within the sponsor's platform, or under contract with a CRO, but still working for a specific sponsor. This interaction is beneficial to the sponsor because the contractors are not entitled for any employment benefits from the sponsors. One of the commonly noticed attributes with this kind of model is that these contractors often don't attach too much expectations for career goals and growth here as they are clearly aware of the limitations. The contractors also may not take on any departmental responsibilities or participate in any of the sponsor's initiatives. The most common drawback to this kind of relationship is that contractors may not stick with the job for a long time, and they are often leave for a better-paying opportunity.

STRATEGIES FOR OPTIMIZING THE PARTNERSHIP

Based on the nature and depth of the partnership, the CRO with fully integrated FSP model appears to be productive and sustainable, with both parties benefiting from each other. The surge of smaller biotech firms with very promising pipelines has been an especially attractive niche in the industry in recent years. Having identified the optimal model of partnership, we can now look into the ways for fine-tuning the partnership to get the best out of interaction and identify the elements that both partners can focus on. Certainly, successful partnerships cover many aspects of clinical trials. However, in this section, we focus on the programming aspects, from SDTM through ADaM and the generation of submission packages.

SCALABILITY OF PROGRAMMING UNIT

Unlike the CRO teams with in-house capabilities that have fairly fixed head counts, FSPs have the ability to scale the number of resources depending the workload on the sponsor's side. However, this needs to be carefully managed. While revenue determination is highly linked to the number of programmers, this would be an attractive variable to be acted upon when there is a restructuring decisions and subsequent workforce reductions. Frequent reductions in the work force and shuffling of programmers across teams or projects disrupt the working environment that programmers have established. Dissatisfied programmers will quit sooner. Here both the CRO and sponsor should carefully identify upcoming deliverables for the period of at least six months ahead of deadlines so as to determine the resource needs well in advance. This approach helps both parties maintain optimal resource balance throughout the contract. This is a vital parameter that both sides must pay attention to, as this creates trust among the programmers, who in turn value their work and demonstrate high level of commitment in their deliverables.

SHARING OF RESPONSIBILITIES AND PROGRAMMING TASKS

While major timelines for a study are set by the sponsor's management, details on the plans for execution and operations according to the timelines are governed by the Senior Managers or Associate Directors or compound-lead level programmers from both sides. A determination of who does what requires clear planning well ahead, especially at the kick-off meeting. At this stage, a genuine sense of shared ownership and responsibility must exist on both sides. Because both sponsors and FSPs carry out 'cherry-picking' approach while selecting programmers for the particular deliverable efforts; well experienced career-oriented programmers from both sides always look for something to learn more and efficiently contribute. General planning covers the activities that may span from dealing with raw data extraction/transfer through completion of eSUB package for a study. Does every part of typical programming product development life cycle require identical approach in terms of sharing of expertise and responsibilities among the CRO and FSP teams? In fact, not! The optimal approach for the partnership can be highlighted for specific portions of the programming can be clarified as follows:

Raw Data and Clinical Data Management. Though it is common to notice that many sponsors outsource the responsibilities related to these areas to the external vendors, still it is a wise approach if the sponsor has its major portion on overseeing these tasks. It is ideal if sponsors can take full responsibility for ensuring the timely execution of tasks relating to raw data collection and its data base management, because these areas require constant data monitoring and frequent coordination across cross-functional teams to follow up on any issues resulting from the data collection steps. Sponsor programmers can handle this step efficiently due to their closer proximity to the cross-functional teams that are directly connected to the raw data.

SDTM. Managing the SDTM development of a study requires a special emphasis for the sponsors. It is very common that a sponsor employs different vendors for developing SDTM and ADaM portions. Hence in these situations, SDTM and ADaM deliverables are carried out by completely two different organizations. Though there can be certain immediate benefits for the sponsors from the cost perspectives, this kind of arrangement may not be efficient in the long run. Following representative scenarios can clarify further:

1. Since SDTM is well evolved and it is common to witness a notion that 'predominantly it requires refreshing of programs being used in all preceding extractions based on mapping that is already in place'. This can easily lead to a SDTM delivery that failed to address a latest change in a CRF that requires an update in the SDTM programming. Many small and newly emerging CROs provide their services on SDTM programming, and their costs are fairly attractive. Biggest disadvantage for this model is the tediousness and the time frame for handling and resolution of data issues at the SDTM level. It is very common that the quality issues are found out during the programming of ADaM datasets or/and review of outputs by the Statisticians. At that stage, coordination among the SDTM vendor, ADaM vendor and Sponsor teams for resolving the issue with SDTM development does take significant level of distraction, time, and efforts in getting the corrected data back.
2. During SDTM development, many information requires closer discussion with Statisticians or ADaM programmers from the sponsor's side. For example, generation of critical date variables in DM, DS and ES domains can represent frequent mapping issues and to avoid the any potential errors at the later stage, the SDTM group must have clear communication well ahead with the ADaM and Statisticians in terms of mapping; in the same manner, ADaM team also may closely work with the SDTM group and verify the algorithms and mapping instructions during the development of critical domains related to important safety and efficacy analysis.
3. Timely communication about the revisions and updates in the CRF, data collections/entry issues across the cross functional teams are very important. Any lapses in the timely transfer of information in these areas can result in a SDTM delivery that included domains wherein latest data collection may be missing.

To avoid this kind of a situation, Sponsors can give the both SDTM and ADaM responsibilities to the same organization (CRO).

ADaM. In general, there is a tendency to assign all safety datasets to the CROs, and keeping efficacy with the sponsor teams. It is due to the assumption that the efficacy datasets require constant monitoring and

updates and also include critical/complex algorithms pertinent to the key endpoints of the study. Though it appears to be reasonable and safe, it is not efficient from the perspectives of utilization of available expertise in the integrated team. Rather, whether safety or efficacy datasets, probably it is an efficient plan to spread the responsibilities of development and validation across the team once a project's programming team comprising of programmers from both aisles have been created. Basically, this is done based on the competency level of programmers and the complexity level of the needed for a given dataset. Ideally in a typical integrated setting, for an important analysis dataset, if the sponsor team carries out the development program, then it will be better to keep the validation effort of this dataset with the FSP programmer. In this way, quality of monitoring is based on the unbiased programming efforts and results will be very reliable. The same logic applies for TLFs programming also. In this way, the competency level of programming as well as knowledge on the key datasets/outputs are evenly distributed among the programmers from both sides.

Submission Packages. Components of the packages (such as Reviewer's Guides, Define Documents, ARM, program text files) can be assigned across the team well ahead. However, there has to be two tier reviewing should happen and, the ultimate review and approval of final quality should lie on the sponsor side.

Integration and Expertise sharing via SME structures. Sponsor must view the CRO's role as a partner rather than as a vendor! This is important and sets the tone for all subsequent steps in the operations. If the sponsor treats the CRO's team as some sort of data-producing commercial teams, the essence of partnership would not appear in their mind and subsequently in the way of handling tasks being handled by the CRO programmers. On the other hand, CRO team contains talented programmers who have gained vast experience from handling multiple therapeutic areas and different phases of trials possibly through working in various organizations.

Regardless of the nature of business, in any business partnership, the volume of benefits that each party brings into the business is a critical factor for the sustainability of the partnership! Of course, element of revenue is critical, but this alone cannot be the deciding factor, though this is the way most of the partnerships are being handled. While sponsor owns the trials and has the privilege of having a fairly well-optimized programming platform and resources, still it may have lapses in its business practices and knowledge in certain steps of the clinical trial processes and programming aspects. If both parties establish a very productive partnership, a long-term commitment for a high-quality delivery is being established. Shared knowledge brings out well streamlined operations and high level of efficiency in handling timelines. Prompt completion of targeted tasks easily reflects cost efficiency as there is no need for re-work of any tasks. Eventually, a productive working relationship based on effective communications and trust is built. This allows both sides to review their experience and comfortably acknowledge the lapses/mistakes, and both parties learn from their mistakes. Success story of a completion of one study sets the tone and path for the subsequent handling of studies. Because it is easy to translate the experiences from one submission to other and this is how a smooth system for sustainable platform is being created.

CRO team caters to these specific needs via bringing their expertise and enrich the quality and beat the timelines. In order to expand and amplify the success of interactions into the rest of the trials or upcoming deliverables, both sides can identify talented resources from both sides and create an SME team for each aspect of the programming. For example, some of the following areas require constant updating and housekeeping for addressing growing programming needs: Monitoring of updates from CDSIC standards and relaying the same across the teams, constant revisioning of the programming platform in line with emerging CDISC Standards' updates, optimizing the proprietary as well as the utility macros in line with the organization's growing standards for their TLFs, upgrading data specification files in the light of versions of SDTM/ADaM Implementation Guides to be adopted, formatting the data specification files for their readiness for the Pinnacle21 tools for Define.XML generation and compliance verification. These areas require the inclusion of handful of programmers with sufficient expertise in both programming and industry knowledge to constantly work on. Though a small number of bigger pharma can afford to have dedicated teams for these areas, certainly emerging small biotech firms cannot afford to have dedicated teams for

these purposes. Therefore, the best way is to create a stable SME structure comprising of programmers from both sides.

How do these SME-groups function and contribute to the high-quality deliverables? It is to be noted that these potential working groups with selected programmers as SMEs would concurrently would work on the updates as per the needs of their programming platform while these programmers would also have their regular tasks under their assignments. Sponsor's management can assign a senior level staff as lead for the specific action group, because both short- and long-term goals of each action group need to be in line with the requirements and areas for the improvement in the programming platform that the sponsor intends to gradually establish. The leads of individual core teams can arrange to meet regularly (at least monthly) to prepare the plans in line with the institution's requirements and assess the progresses being made. Whether a smaller biotech or a bigger pharma with a programming platform with necessary talents in place, both CRO and sponsor teams, can start thinking of establishing SME (subject matter expert) groups comprising of programmers from both sides with long term goals. Sponsor can cherry pick experienced programmers from the CRO side based on their interests/expertise, and embed them into its SME team. This not only captures the high level of competencies of the programmer but also programmers consider these steps as empowerment and rewards for their contribution. In the long term, this will help in retaining of best work force on both sides. In our experience, this kind of joint efforts in creating SME structures have produced fruitful results in terms of maintaining updated standards and quality compliance and timely deliverables. Hiring programmers for immediate programming needs and ending their contracts once the jobs are completed is mere transactional though both teams work in collaborative mode. But utilizing the skillsets of existing programmers to improve the programming platform in the areas such as the generation of TLF/Utility macros, improvement in meta data managements, enhancing CDISC compliance in both SDTM and ADaM programming, etc. will help the sponsor company get ready for the next level of technological growth. While these are the immediate benefits to the sponsor team from these successful initiatives, the programmers from the CRO team will feel more empowered when their actions are contributing to the sponsors programming platform.

NEED FOR A VISIONARY LEADER TO HEAD THE PROGRAMMING TEAM

It is essential for a sponsor to have transformational leader, not as a mere programming task manager, as a head of the programming platform. This is very important especially when the sponsor is a small biotech firm that has plans to advance their promising drug candidates to their late-phase clinical development stages. In this context, it is essential for the sponsor to have a visionary individual to lead the programming team because actions and thought processes of the head of the programming team must reflect the high-level plans that the senior managements lay out for the upcoming years. The head of the programming team in turn must be in a position to relay company's goals and navigate the core teams in garnering efforts to create the foundation for the updates. He must be in a position to identify the talents from both sponsor and FSP teams, and foster the way to nurture a positive and collaborative culture so that the CRO/Sponsor partnership stays stronger and very productive.

CONCLUSION

As long as the clinical drug development continues, the need for the clinical and statistical programming tasks and work force needed for these areas are going to exist! Both CROs and sponsors will have requirement for the resources to carry out the task. The question is which side hires more programmers? Regardless of the models under which CRO/Sponsor partnership is pursued, partnership will continue. Industry has witnessed a fluctuating scenario in terms of outsourcing pattern of programming tasks to the CRO by the sponsors. A sponsor can outsource most of the programming tasks (both SDTM and ADaM) to CROs for a few years and then decide to cut down outsourcing needs and start thinking about creating their own in-house programming team. This cycle continues. One of the reasons behind these fluctuations is that lack of clear planning on logistics of sharing responsibilities among the partnership and also lack of closer monitoring and nurturing mechanisms during the partnership! As explained earlier, the best strategy for sponsor is to have good team for programming on their side and concurrently engaging with CROs in

an integrated FSP model for the additional support with cherry picked talents, in this way, there will be an optimal level of engaging and dis-engaging between the two. Also, it will be convenient for making any potential restructuring decisions, due to certain inevitable business outcomes. The best sponsor-CRO sponsorship is a collaborative and mutually respected partnership.

REFERENCES

https://www.clinicaltrials.gov.

https://www.cdisc.org/standards.

McLaughlin, S. 2021. "How to handle decision making in the CRO/Sponsor relationship in matter that require expertise". *Proceedings of the PharmaSUG2021 Conference., USA.*

Evans, C. and Kennedy, S. 2022. "How Clear Communication & Expectations Improve the CRO – Sponsor Relationship: the CRO Perspective". *Proceedings of the PharmaSUG2022 Conference*, Austin, TX. USA.

Matthews, C. 2022. "Empower Your Programmers: Get the Most from Your Programming Team". *Proceedings of the PharmaSUG2022 Conference*, Austin, TX. USA.

Matthews, M. 2015. "A Similarities and Differences in Statistical Programming among CRO and Pharmaceutical Industries". https://www.lexjansen.com/phuse/2015/pd/PD02.pdf

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