Paper SP10

Common Misconceptions from Sponsor's and CRO's Programmers & Their Challenges

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ABSTRACT

The purpose of the presentation is to share insights to build stronger collaboration of programmers between CROs and their sponsors. This will lead to long-standing, shared partnerships through the shared commitment to help patients. There are two parts of this presentation. First, we address some common misconceptions around timelines and delivery where the related misunderstandings might result in frustrations from both sides, and how this can be avoided. In the second part of the presentation, we identify a list of roles, responsibilities and challenges we face as programmers from both Pharma and CROs. This can help programmers understand the expectations and come up with strategic programming plans to work in collaboration with each other and achieve the timeline with minimal budget and higher quality.

INTRODUCTION

The co-authors have worked in big and small, established and start-up, pharma and CRO environments as SAS programmers for years, and have been fortunate to gain valuable hands-on perspectives from both sides. Based on personal reflections, as well as conversations with our colleagues, we will present some of the key areas of misconceptions and offer suggestions to improve collaboration between pharma and CRO programmers. Also, we will provide a list of different focus and challenges on pharma and CRO environments.

MISCONCEPTION FROM CRO PROGRAMMERS

1. One misconception from the CRO's side is that surprising the sponsor by making deliverables extremely early shows their dedication and is a benefit to the sponsor.

Author's perception:
The truth is the earlier than scheduled delivery by CRO programmers might not be a benefit to the sponsor's programmers, especially on planned and non-urgent deliverables. There are two reasons from the author's point of view and experiences. First, the sponsor's team might have other priorities and may not be available prior to the scheduled time to review or provide feedback on the deliverable. Second, if the sponsor's team receives the deliverable early, they might be forced to change their timelines accordingly. This might result in an internal timeline negotiation, not only across programming and statistics, but also across other functions within the company.

Suggestion:
Unless the sponsor expresses a preference to receive the deliverable as soon as possible, CRO programmers should not deliver deliverables well in advance of the due date without confirming that is what the sponsor wants. In cases when CRO programmers can have the delivery ready significantly earlier than the planned date, they should communicate this to their counterpart as soon as possible and ask for confirmation on whether they would like to receive the delivery right away and whether an adjustment is needed for the downstream timeline. This communication will allow the sponsor's team to anticipate any possible schedule changes and avoid a situation where the sponsor's programmers have overlapping tasks. The bottom line is sponsors are expecting to receive planned deliverables on the scheduled day unless otherwise communicated, so make sure to communicate any changes to the timelines.

2. Another misconception from the CRO's side is that they expect sponsor's programmers to include the root cause analysis in the feedback when discrepancies are identified by the sponsor's programmers. The reason that this is a misconception is that the sponsor is usually paying the CRO to do validation but not to resolve discrepancies with the sponsor. CRO programmers are assigned to work on each study within a limited time frame and usually the programming and validation hours are used up working with internal CRO validators.

Author's perception:
If CRO programmers fail to include programs, logs and datasets in the delivery, it is likely the sponsor's programmer will not be able to investigate discrepancies between the CRO and sponsor outputs. This creates additional back and forth discussions, and a lot more work and frustration from both sides to address the root cause, and to find an effective correction.

Suggestion:
Including programs, logs and datasets (when appropriate) as part of the deliverable will increase efficiency and cost saving from CROs.

3. Another common misconception is that CRO's programmers expect that the sponsor is sure the CRO is wrong when they point out a mismatch between sponsor and CRO results.

Author's perception:
A sponsor may question results from the CRO for many reasons. Sometimes a simple question is exactly that. For example, a question about why a table doesn't match another table or listing may be answered by pointing the sponsor to a title that describes the subset of the population or time interval or a footnote that explains the unique results of an output. Sometimes a question about how a derivation is calculated is a request for the logic behind the derivation, not a request to change or re-evaluate a derivation. Sometimes the sponsor physician may ask the sponsor statistician a question which trickles down to the CRO programmer through perhaps the CRO statistician or sponsor programmer so the intent of the question may be lost by time it

gets to the CRO programmer. Questions from the sponsor may lead to identification of SAP, spec, raw data, analysis dataset, or programming issue but sometimes sponsor questions are simply a request for information.

Suggestion:
If it is not clear then clarify why the sponsor is asking the question (e.g., has the sponsor identified an issue or is the sponsor seeking clarification). If a question is merely a request for clarification or information, there is no need to make spec or programming changes unless the sponsor requests modifications.

4. Another common misconception from the CRO's side is that comments made by the sponsor's programmers or statisticians should be incorporated exactly as made and without asking follow-up questions.

Author's perception:
The sponsor's programmers and statisticians are human and therefore subject to a variety of errors or lack of clarity in communication. Sponsor employees have a diverse range of knowledge about therapeutic areas, study intricacies, previous study decisions, compound standards, and even their own SOPs, as well as written and verbal communication skills. In an environment where sponsor employees may move to new opportunities every few years but CRO employees stay on projects until they end, it is not uncommon for some CRO programmers to have much more experience with a study (and maybe even a sponsor's standards) than sponsor programmers. In such cases, the CRO programmers may be able to educate the sponsor's programmers in some areas.

Suggestion:
If a sponsor programmer makes a request that is unclear or seems to contradict previous decisions, study documents, SOPs, industry or therapeutic area standards, or common sense then the CRO programmers should feel empowered and obligated to ask for clarification, referencing the appropriate study documents when necessary. This will reduce re-work for both the sponsor and CRO while increasing quality and reducing cost.

MISCONCEPTION FROM SPONSOR'S PROGRAMMERS

1. A common misconception from the sponsor's side is that some believe CRO programmers have no budget or time limit when working on a study.

Author's perception:
CROs focus on quality and maintaining tight budgetary control in order to provide a high-quality deliverable at a fair price. Most CROs have a business model that involves managing budget by hours in order to maintain the revenue balance needed to sustain itself.

Suggestion:
Sponsors and CROs must work together to ensure that changes to analysis specifications are made with caution. This includes being cautious when suggesting updates, especially non-critical ones, and going through the correct channel to request updates. Excessive small changes, multiple rounds of comments, change of mind, and

unconsolidated comments often lead to inefficient use of time and funding for all concerned.

CRO programmers are working hard to complete deliverables according the timeline and budget constraints. Requests for changes at the last minute, or after the scheduled review period, puts pressure on the CRO programmer to work overtime, to deliver customer satisfaction. Going through the correct channel to make requests alleviates some of this pressure, as does providing timely and accurate review feedback and encouraging sponsor colleagues to do the same. Having accurate timelines and budget for the amount of reviews needed for a project is also critical to success. It is the author's experience that physicians like to give the bolus of their comments at the end when data is more complete, and tables and listings can be compared so considering this when drafting timelines will help make sure the CRO has enough resources to handle the workload.

2. A second misconception from the sponsor's side is that subsequent Independent Data Review Committee (IDMC) reports won't take much time or effort because they are repeat work, only needing simple adjustments.

Author's perception:
It takes much more time than you might think to update the programs for the subsequent IDMCs. Because on-going data collection is usually very messy, especially for studies where data collection is complex, new visits are being included in the IDMC, or the study team is making data collection or cleaning adjustments as the study is ongoing. For every IDMC update, CRO programmers must face various unexpected data issues, raise a query to the Data Manager, and perhaps re-program to accommodate new data values. This makes the downstream programming work much more challenging and time consuming than it seems like it should be.

Suggestion:
Don't expect perfection for the IDMC reports but focus data cleaning efforts on important endpoints. If data issues don't have an impact on the decision making with respect to the particular IDMC objectives, then be willing to accept that the data will not be as clean or complete as it will be for a final database lock. Please note, the IDMC members understand the reports are from the on-going studies, and it is very common to retain data issues or imperfections for IDCM reports.

3. Another misconception is that sponsor programmers think CRO programmers are dedicated full-time on their study.

Author's perception:
The misconception here is in thinking that CRO programmers are only assigned to one study. Except in contract or Full-Service Provider (FSP) outsourcing models, CRO programmers are not necessarily dedicated to one project or sponsor but may work on multiple projects. The standard CRO model is for sponsors to send work to a CRO and the CRO management will assign and manage resources working on a project. There are times when it is more efficient for programmers to work on multiple projects and the CRO management is responsible for allocating the resources in such a way to deliver on all contracted work.

Suggestion:
Keep in mind that CROs may have multiple clients or projects and are working towards the agreed upon timelines for all of their projects. If you have specific expectations, it is best to communicate those and incorporate them in the timelines and contract.

4. Another misconception is that the CRO programmers work on deliverables in equal proportions over the time allocated to finish the deliverable.

Author's perception:
As mentioned previously, programmers are not dedicated to one project or sponsor but work on multiple projects. In order to allocate resources efficiently, project work is often back loaded to give time for specs to be finalized and projects with earlier deliverable dates to be finished before the full team of programmers start working on a project. This avoids downtime caused when programmers move to a project before the team is ready for them.

Suggestion:
If you have specific expectations for the progress of deliverables, it is best to communicate those and incorporate them in the timelines and contract.

5. Another misconception is that because CRO programmers work on multiple projects and the CRO is paid the same regardless of the success of a compound that the CRO programmers don't care about the overall success of a compound but just want to get their part accepted by the client with the minimal effort.

Author's perception:
CRO programmers care about the overall success of a compound for both personal and professional reasons. The obvious example is that it is helpful to a CRO programmer's career to work on approved drugs and have good client feedback but the interest in success of a drug goes far beyond just padding a resume. Often programmers ask to work on drugs in certain therapeutic areas because they know people suffering from a disease in that therapeutic area. Helping get drugs to the market is personal when you can put a person you know in the place of patients who may benefit from a drug. CRO programmers also experience satisfaction from helping to get drugs to patients and of a job well done just like sponsor programmers do. One author has worked on several compounds that were reported on national news after pivotal results were announced and again after approval by the FDA. Often it is hard to explain to family members what we do for a living, but people know we are doing something important when we are part of getting a drug to the market that is touted on the national news as a breakthrough in treating a condition.

Suggestion:
There are legal reasons why contract and CRO programmers need to be treated different than sponsor programmers but try to find a way to include CRO programmers in acknowledgements about the success of the submission and the potential benefit to patients and shareholders the drug may bring. Small things like forwarding congratulatory emails to the CRO programmers from upper management, taking time to thank the programming team for their effort and reminding them the impact they will

have on patients, or having an upper manager call in for the first 5 minutes of a sponsor/CRO meeting to thank the sponsor and CRO team for their effort are easy and cost-free ways to show appreciation without violating HR policies or employment laws.

TIPS ON EFFICIENT COMMUNICATION

To CRO programmers:

1. Be open. Don't be afraid to ask questions and get clarification from your sponsors' counterpart. This is especially important for the initial studies or a new concept in a series of studies. One author recalls when she worked on the sponsor's side and needed clarification on a little thing. She picked up the phone to call her CRO counterpart and could feel the programmer on the other side of the line was very nervous talking with her. That made her feel guilty and never want to call again. Remember, in general, the sponsor's programmers are willing to work and help you anyway they can, because we are all on the same team to make the study run smoothly.
2. If your questions pose significant risk to the timeline, request a response within 24 hours in the email. If needed, set up an ad-hoc meeting with your sponsor's counterpart.
3. Don't be afraid to raise your concerns as soon as you foresee a danger of missing timeline. The time to consider contingencies is when you still have time to enact contingencies.
4. Be informed. Review study documents and ask other CRO employees general questions before you ask sponsor programmers. The CRO, not the sponsor, should get new CRO employees up to speed.

To sponsor programmers:

1. Treat CRO programmers as one of your colleagues, including using a respectful attitude to communicate with them.
2. Be constructive when you provide review comments.
3. Inform the CRO programmers if the CRO has worked on a sister study that may be used as a template. Also point out differences between similar studies that may not be obvious (e.g., difference version of CDISC or internal standards, change in derivation of endpoint).
4. Get clarification on scope, timelines, and who you should contact at the CRO for different types of questions (e.g., programming, specs, data, contract, timelines, escalation) and who all needs to be copied on emails.

COMPARING PHARMA AND CRO PROGRAMMERS

The following table helps to delineate differences between CRO and Pharma programmers by roles, responsibilities, and challenges.

	CRO	**PHARMA**
Broader view	Work with dynamic clients across multiple therapeutic	Get to see the full clinical study picture and have a broader drug

	areas to develop a broader skillset and flexibility	development experience. Programmers have been involved in clinical trial development, have input in the protocol, SAP, CSR, & CRF, attend meetings and communicate directly with medical, regulatory, and clinical teams, and program for regulatory responses.
Challenge	Uncollated/unconsolidated comments from a variety of sources at the sponsor, leading to challenging/aggressive timelines	Pressure of working on ad hoc reports, publications, exploratory analyses, and quick turnaround regulatory requests, while lacking programming infrastructure and deep understanding of details of the programs when studies are outsourced. Being responsible for delivery of outputs with no direct authority over CRO employees doing programming. Doing oversight without direct access to CRO programmers, maybe not even knowing who or where the programmers are.
Standards	Exposed to a much larger variety of drugs, indications, and company standards and need to apply the CRO standards flexibly to meet sponsor requirements	Use the standards and tools from only one company
Financial Management	CRO functional leads need to account directly for the financial health of their projects.	Management of budget is often done at a higher (e.g., compound) level.
Career path	Technical and management tracks based on skills more than degree or ability to succeed at office politics. More opportunities for advancement in technical track.	Can manage the work being done by others without management career track. More opportunities to focus on innovative solutions or solving new problems instead of using existing tools to program datasets and TLFs.

CONCLUSION

It is quite common in the industry for SAS programmers to move throughout their careers into a combination of sponsor, CRO, and/or contractor roles. No matter where we go, keep the growth mind set. Regardless of where we work, CRO or pharma, we as statistical programmers all have the same accountability to compliance and commitment to the clinical research. Hopefully this paper can help programmers to be more

collaborative, and to understand more of each other, and be willing to take some risks and challenges.

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