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Building a Partnership: Constructing a global team between a US Sponsor and a Chinese CRO

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ABSTRACT

There may be many reasons for a sponsor to decide to work with a CRO but no matter the reason both teams always want to ensure a successful collaboration. Careful planning prior to the study work beginning is an important step towards this goal in any situation, no matter where the companies are located, but when they are in different countries planning becomes imperative. Whose SOPs will be followed? How will issues be communicated? What are the responsibilities of the leads within each company? By discussing, and coming to agreement, on these types of questions before study work starts, the teams avoid slowdowns due to confusion, miscommunications and under realized expectations. To avoid these issues Santen and Rundo teams have worked together to construct a solid plan prior to study work getting underway to clearly set expectations, anticipate challenges and develop processes to mitigate identified risks. This paper is intended to describe the steps taken and the working model for the partnership that resulted from these discussions.

INTRODUCTION

Santen is a pharmaceutical company dedicated to the ophthalmic fields; Santen carries out the research, development, sales, and marketing of pharmaceuticals. The company has 15 bases in 12 countries globally, to include its US subsidiary, Santen Inc. in Emeryville, CA. As a leading company in the field of ophthalmology, Santen aims to contribute to society by supplying valuable products and services to satisfy unmet medical needs. A little over a year ago, Santen Inc. Biometrics leadership decided to engage a CRO to assist with programming tasks for current and future studies. Beyond a simple "need based" search, we really wanted to identify a "partner" in our study development and therefore looked for a company that was open to a role based working model, as opposed to task based. In other words, a company that was willing to provide dedicated programmers to Santen studies that would engage them at the same level and ownership as that of a Santen employee. In Rundo we found such a partner and who was equally dedicated to both quality and the success of the partnership. Rundo International Pharmaceutical Research & Development Co., Ltd. (Rundo), founded in 2004, was the first Sino-foreign joint venture CRO (Contract Research Organization) in China. Rundo provides professional clinical research outsourcing and post-market consultancy services and is based in Shanghai with branches located in Beijing and a subsidiary clinical data management (CDM) center, which includes their programming staff, in Nantong.

The two companies worked together to put into place a contract that outlined the aspects of the partnership within a Function Service Partnership (FSP) model. The model specified the partnership as one where Rundo would hire and manage a group of SAS programmers to work solely for Santen. Fees would be paid on a fixed annual basis, rather than by project. It also specified that programmers working at both Santen and Rundo would do their programming tasks within their local system while data, documentation, and outputs would be shared between the two teams via a secure FTP server. It also specified, under this model, Santen's SOPs would be followed by the designated Rundo team. As they would be treated as Santen workforce members and thus should be part of government audit, we developed a plan for Rundo team members to provide training on Santen specific processes and procedures in addition to the training they received as Rundo team members. This training would be provided through on-site training in Nantong, as well as bringing Rundo programmer to work on site in our US office to work with the team directly. These decisions gave a good foundation for the study work, however there were still many questions that needed answered, specifically related to how study work would be conducted between the two groups on a more granular level. This required an assessment of how the work would be done, what each team's responsibilities were on a study, how issues would be addressed, and other factors the teams would face in their day-to-day tasks. We felt planning was required for mapping out these factors and in turn would set the team up for successful outcomes for the work ahead. One advantage we had was that leadership on both teams had experience in similar situations that could help recognize and identify pitfalls that would have an impact on the teams if clear processes were not in place

before work began. To capitalize on this we went to work to develop processes and procedures that the global team would follow to guide them if and when challenges were encountered. This paper describes some of the key areas we felt were critical to the success of the study work; task management, communication, and process consistency. It also provides the “plans”, or work processes, we decided to implement. While the risks, and resulting processes, discussed in this paper should not be considered an exhaustive list, it is our hope that by sharing these examples others could use them as a starting place when building their own global teams.

PLANNING

First a little bit about the planning process itself. In general, programming tasks are similar whether working on the sponsor or CRO side. So when working together it seems simple, programmers will program and planning takes time, time that could be used to get some tasks completed. While this is true, it is our opinion that the time spent on planning is time well spent. Without planning each party will go into the task with their own ideas and assumptions of how things will work and what will be expected. Something as simple as how issues are communicated can cause confusion when one team sends all issues to a single person, but the team on the receiving side is expecting everyone to be copied. Does the receiver know to share the information or will it create a ‘bottleneck’ as they try to address everything themselves? What measures are in place to prevent issues from getting lost or overlooked? Without a clear and agreed upon process, the progress of the task with the issue could be in jeopardy. Additionally, areas of concern for one team may not be known or considered by the other team might have. Again, a simple example would be holidays, which can be different from one company to the other. Do both teams get Christmas week off or only specific days around the holiday? That is why we also stress that this should be a joint effort to provide robustness and benefit to the team as a whole. We also recognized the fact that this was not a one-time decision making process. It is admittedly difficult, if not impossible, to identify every challenge that will be encountered and that, as study work began, we would likely need to make modifications to our initial planning to continue improvement. We saw the process as a cycle (Figure 1):

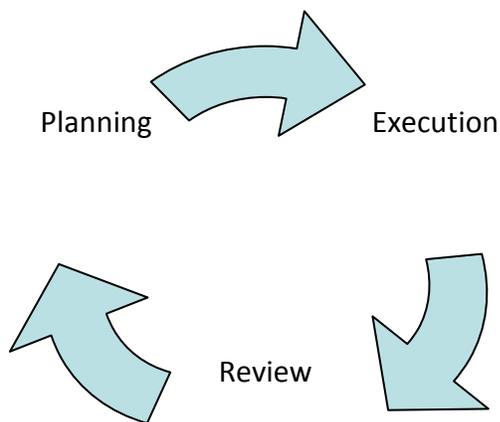


Figure 1: Process development cycle

For the purpose of developing a working model (processes), the planning phase encompassed two parts; identification of risks and determination of how these could be mitigated, if not eliminated altogether. Once completed, the process moves into the execution of the work utilizing the planned processes. Review would be completed and comments shared through feedback. If changes were needed to the plan or new processes needed to be developed for situations not accounted for, the cycle would start again with the issues being discussed and the initial processes updated. The Santen and Rundo team are now working on their first project together, and while this type of assessment of the initial plan is underway, the planning phase will be the focus of this paper.

TASK MANAGEMENT

One apprehension facing any company when off-site resources are used is how work will be managed, especially when those resources are within a different time zone. There are advantages of course when you consider this allows work to continue during periods an on-site team would not be working. However the management of the tasks

has to be carefully organized to ensure there is no overlap in effort, progress is acceptable, and that issues are resolved as quickly as possible. If the offsite resource is a single telecommuter small adjustments in management processes may be all that is needed. But the challenge becomes more complex when tasks are shared across multiple teams; it becomes critical to ensure everyone is working towards jointly agreed upon goals. To be clear the management of the tasks is different from the management of the team members themselves. As specified above, the contract set forth between Santen and Rundo covered the latter point; the local management would have the responsibility of management of the individual team member, such as reviews and career development. While cross site feedback may be given for these activities, the focus of our assessment was management of the tasks, specifically the oversight and assignments of the tasks, and combating the time zone differences.

CLEARLY DEFINED ROLES

Before work begins, members of any programming team should have a clear understanding of what role they will take and hence what responsibilities they will have for the study work ahead. This is especially true for a cross site team as it gives structure and provides escalation points when trouble arises. We outlined the following structure for our team (Figure 2):

Role	Location	Responsibility
Lead Programmer (LP)	Santen	Programmer responsible for all programming activities on the study to include, but not limited to, oversight of timely task completion and the quality of the output. Lead programmer would additionally perform study tasks critical to the success of the study (e.g., efficacy programming)
Lead Programmer (LP)	Rundo	Programmer who would act as the primary contact between Rundo and Santen and work with the Rundo manager to provide oversight for the study team at Rundo. Lead programmer would additionally perform study tasks critical to the success of the study (e.g., efficacy programming)
Study Programmer(s)	Santen/Rundo	Programmers who would perform the study programming itself.

Figure 2: Study Team Roles

As for site-level management's roles we agreed the Head of Programming at Santen would maintain the overall responsibility for the study but would work closely with Rundo manager to ensure study progress was appropriate and to reach resolution of any study level issues.

ASSIGNMENT OF TASKS

Though a benefit of a global team can be the distribution of work to alleviate pressure on one team or both, we realized it would be difficult to have one-directional work assignments, for instance having the Santen LP assign tasks to all programmers on the team. The difficulty with this process was largely due to the recognition that, as the team was working together for the first time, the skill level of all programmers might not be known to the person making the assignment. This would not allow efficiencies to be capitalized on. Additionally, if a team member completed their work early in their day, without another assignment, it could take an entire day before a new assignment could be given if the person making the assignments were at the other site. It simply would not provide the flexibility needed to ensure timelines were met. Instead the Santen LP would identify the tasks to be covered by the Santen team, and make the assignments for those tasks, and then the Rundo manager or the LP at Rundo would make the appropriate assignments for the remaining tasks. This would allow work to continue, and shift work as needed, to ensure the completion of all tasks.

One key factor to work assignments was "what" assignment was being given to the Rundo team. As we embarked on our first project, we recognized the Rundo team would need to get familiar with Santen's processes, beyond the training that was provided. We decided to "ramp up" the team by giving them select assignments that would gradually increase the complexity and scope of what they worked on. By gradually increasing the complexity we felt it would allow them to get familiarity and comfort with the processes and the study. Then as their comfort level grew they could take on a larger portion of the overall scope of work.

We also assessed what the tasks entailed to reach completion. For example, due to the requirement that key outputs were to be double programmed according to Santen's processes, a single output would be comprised of two tasks, a source program and a validation program being developed. Time delays between the source and the validating

programmers would impede the progress. We decided to avoid time and distance issues we would, as much as possible, ensure all tasks for an output would be assigned and completed at the same location. This could change if there were priority or resourcing shifts, however the initial assignment for an output would be maintain on a locational basis.

PROGRESS OVERSIGHT

Being a multi-locational team, we knew it would be essential to have a process in place to track the progress of tasks to ensure teams got assistance when needed, and ensure the timely completion of the tasks. We knew how issues are communicated; tracked and resolved can have a direct impact to how well this is accomplished. A tracker (spreadsheet) was agreed upon as a centralized document for both teams to use to communicate the status. It would contain a record for all items the programming team will create from the specifications and planned outputs (SPTOC); datasets, tables, listings, and figures (TLFs). It would also provide a single place where assignments, program names, and comments/questions/issues could be kept. It would be the Santen LP's responsibility to create the initial tracker, which would then be shared between the leads, with updates made and shared between the two at the end of each day. The comments/questions/issues kept here would be initialed and dated so that the responses could be directed appropriately and monitored for resolution. We also specified that if discussions took place through email, or other forms of communication, notations would be added to the spreadsheet if resolution was not achieved during the outside conversation. An example of a tracker follows (Figure 3):

Task	Source	Source Program	Status	Validator	Validation Program	Status	Notes/Comments
ADAE	Prog A	adae.sas	Complete 7/25/14	Prog B	vadae.sas	Ongoing	Note update to specifications [progA 7/25/14]

Figure 3: Task tracker example

WORK SCHEDULES

The Santen team is in Emeryville, CA, and the Rundo team resides in Nantong, China, which makes for a difference of sixteen hours. As previously mentioned, this can be an advantage. In our case, the time difference can provide progress to continue on a study almost around the clock for four days of the week, with each team contributing an additional day at each end. However it can be a disadvantage when information needs to be shared or a question needs to be address for work to continue. If a question is asked by a team member on one day, at a minimum it will likely be the next before a response can be received. The risk to the task increases as the delay in response increases. While the time delay could not be completely overcome, we decided instead to take advantage of the potential for overlap. For team members at Santen, staying till 6:00 meant there would be an hour overlap with programmers starting their day at 8:00 at Rundo. Or being open to a quick call on Sunday night would mean the Rundo programmer would have an answer at the start of their day on Monday. These adjustments may not be needed on a full-time basis, but we agreed to support the possibility, especially during critical periods of the study.

Works schedule considerations must also include the risks caused by periods outside the regular work hours and extend to special scheduling considerations such as weekends and holidays. If agreements are made regarding timelines without taking into consideration the full team's schedules, expectations can be set for completion that are unrealistic without undue pressure placed on the team. Take for instance if a database lock was moved up from a Monday to a Friday, US-time. While it is a seemingly small change, if tasks were needed from the Rundo team, they would not be back to work for another two days. There is always the risk that due to timeline shifts, changing priorities or other study related needs, that work would be needed during periods the other team was unavailable. While these situations may not always be in our control we determined any shifts would be reviewed, and the impact discussed, as a team before an agreement would be made to avoid expectations being set that could not be met. Additionally, we saw that if a request/change was needed immediately it would likely come from within Santen, requiring the Santen programmers to have access to the Rundo programs to complete the task. To ensure this would be possible, Rundo would provide their programs as part of the delivery of outputs when uploading the "final" version to the FTP server.

COMMUNICATION

Ask anyone to name the challenges of working within a team (anywhere) and its likely communication will be near the top of every list. But add to that locational and language difference and the challenge can grow. Poor communication can have a serious impact on a study by wasting time and effort for everyone involved. Experience of

working with team members may provide an understanding of expectations and allow abbreviated messages as a question or response however that is seldom the case when working together for the first time (and sometimes for some time after) as we would be. A request for someone to “take care of that” at this point in working together could have a different meaning, or not be understood at all, by the receiver beyond the understanding they need to do “something”. Poorly timed responses could cause delays in progress, and unclear requests, or unshared information, could lead to unknown or unmet expectations. We wanted to ensure communication paths were available and clearly stated and that there would be no wasted effort by doing something counter to what is expecting, or worse, causing progress to be stalled when additional clarity was needed.

COMMON LANGUAGE

As a common apprehension of teams working together from different countries, the language question was addressed by simply agreeing on a single language for all communications between the teams. As English is the language in which Santen does business and with all Rundo team members proficiency, which is not the case in the reverse, English was agreed upon. Both teams also had the support of strong dual language speakers to facilitate any gaps. To address clarity, teams were also reminded to use as much detail in their communications as possible. The use of screen shots, spreadsheets, stepwise instructions, examples and anything else that could facilitate a clear understanding were highly encouraged to ensure comprehension of the message.

COMMUNICATION PLAN

Regardless of how determined a team is for all to go well, issues will arise during a study that needs to be addressed. They can be as simple as a question that needs answered for the task to progress, to a full change to the planned analysis. A communication plan would provide all team members the information they needed to connect with the person they needed to share information with. At the start of the study, a communication plan would be developed to identify team members, role on the study, provide contact information for all team members. The role designation was important, though we made it clear the communications should be sent to the person or persons directly affected by the communication, we also set the expectation the leads for both teams would be copied on all communications. This would provide a single, consistent, point of contact that will be copied on all communications to ensure consistency and timeliness of responses. Below is a simple example of the communication plan (Figure 4):

Team Member	Email	Role on Study
Programmer A	aprogrammer@santeninc.com	Lead Programmer (Santen)
Programmer B	bprogrammer@rundo-cro.com	Lead Programmer (Rundo)
Programmer C	cprogrammer@santeninc.com	Study Programmer
Programmer D	dprogrammer@ rundo-cro.com	Study Programmer

Figure 4: Communication Plan

Expectations of escalation paths would also be shared with the team. Any issue that impacted the quality or on-time completion of a task would be communicated to the Head of Programming at Santen and the manager at Rundo as early as possible. This would allow the time needed to have the issue assessed and addressed to avoid the delay or to be communicated to the Santen stake holders if the delay is unavoidable.

WEEKLY TEAM MEETINGS

Though individual communications would occur we also felt it would be important to have a global team meeting once a week to share information and statuses, as well as promote a team environment between the groups. This was a challenge due to the time differences, however once again we decided to take advantage of the overlap period. Weekly team meetings would be scheduled on Monday at 5:00 (PST). In addition to standing agenda items, such as timelines and status updates, it would be used as a platform for questions to be raised and answered and any information to be shared with the team as a whole. We decided to use a combination of web conferencing (with video) and teleconferencing (audio), to provide the opportunity for team members to associate “faces with names” and to give the “feel” we were in the same room. Meetings summaries would be provided by the Rundo team after each meeting and reviewed by the Santen team. This would be to ensure agreement and demonstrate understanding by both teams as to what was discussed and actions that are needed.

SAME DAY RESPONSE

The potential overlap still provided very little time to make direct connections between team members when responses were needed. Work could be stalled or continued inaccurately when delays were encountered. To alleviate this as much as possible, we clearly defined expectations of timeliness of the responses as the “same day as received” to ensure the sender would receive the response at the beginning of their next day. If this would not be possible, team members would be expected to send some form of response to the sender, as acknowledgement the message was received and issues or status of the full response.

PROCESS CONSISTENCY

As previously discussed, the contract specified the Rundo programmers working on Santen projects would follow Santen’s SOPs, but SOPs are meant to be general and an overview of processes. Work processes describe how the work is actually done. Consistency of output can be a challenge between any two programmers and without guidance they must rely on their own experiences or interpretations to complete tasks. Take for instance programming of a table against a predefined shell. The shell has a general placeholder for a line where statistics are presented with a “XX.X” for the placeholder. If the programmer follows the shell literally, the output would reflect a single decimal place. Differences this cause during validation would be addressed between the programmer on the other side of the task, and as described they would be in the same location. However what about ensuring the consistency across all the outputs, are all outputs following this method? To reduce confusion we determined some “best practices” needed shared to further detail the processes described in the SOP. As the studies being worked on needed to be consistent with previous studies performed by Santen, the work practices at Santen were reviewed and updated to accommodate the global team.

PROGRAMMING GUIDANCE

Though the preference is that any modification to programs would be completed by the original programmer, which is not always possible if resourcing constraints require reassignment. As work would be shared globally on our projects, and there was the potential one team would have to take over programs from another team, we felt it was important to have the programs have the same structure and follow the same guidelines. For instance if a program was named ABC.sas and the original validator named their program vxyz.sas, if a new validator is assigned to make modification there would be confusion before work could even start. What if the programmer is used to little to no white space, a lot of time could be wasted trying to find the appropriate code needing modified for someone coming in after them. Santen had an initial document in place for programming standards but working together we developed a more comprehensive one that included such things as use of white space and naming conventions, but also a header template, guidances on commenting, and using RUN after each statement (though it’s not required for SAS® to run).

DISPLAY STANDARDS

Similarly, consistency within a study package can only be ensured if standards are put into place. If not, programming will move forward and, once tasks are completed, issues found during cross output comparisons additional effort is required on a completed task. If the displays are dependent of the preferences of a study level individual (lead programmer or statistician) that differ from someone on another study, contradictions can also be created and when another study is started and the previously understood standards are followed, again resulting in work needed on something that was already completed. Pre-study discussions could limit this however setting standards for displays would ensure everyone has the same expectations. The display standards we created not only addressed decimal issues, to avoid the situation described at the start of this section but the display area to be used, font size, handling missing values and block structure, to name a few.

VALIDATION PROCESS

A programmer that has experience in the industry could assume validation automatically means double programming, however, while everything must go through a validation step, it is not necessarily true it has to be double programmed. Santen’s lead programmer and statistician determine the validation level at the start of the study for each task as manual validation (Level 1), programmatic validation (Level 2) and for key output an additional stat level review (Level 3) that is more in-depth than the content check for the others. However even with the Level 1 review, there is room for inconsistencies if one programmer implements this by producing the content of the output and does a visual check, while another checks a certain percentage. We realized that this too needed further clarification (Figure 5):

Validation Level	Validation requirement	Specifications
Level 1	Manual review	10% of the output's content will be verified against the source data
Level 2	Programmatic review	Validator will reproduce the content of the output and perform a PROC COMPARE against the final dataset used to produce the output. Comparison results will be stored as documentation
Level 3	Senior Statistician review	Senior statistician will perform critical checks, to include but not limited to programmatic checks, on the output contents

Figure 5: Validation designations and specifics

This would aid the team in ensuring the appropriate effort was used for the validation of a task they were assigned to and that could be assumed completed when output was released.

CONCLUSION

The reasons 'why' a sponsor decides to work with a CRO can vary as much as the scope of the work that is being contracted, from a single task to a full partnership. Regardless of the 'why' or scope, the decision can carry with it challenges not outlined in the contract between the two companies. Separation of the teams that introduce language barriers and time zone differences can be obstacles to the day-to-day work performed by the global team. Santen found a partner in Rundo to share the workload as well as the vision for the success of Santen's studies and that partnership started at the management level with a shared view that planning for eventualities encountered in their own experience could provide guidance to the team if they were encountered. This paper outlined some of the overall categories we addressed; task management, communication and process consistency. In addition to some of what issues we could encounter within these categories we gave described the processes we implemented to address them.

After explaining a bit about the planning process itself, we looked at some areas with the task management category. Clearly defining role definitions ensures structure and responsibilities to the team. The assignment of tasks are determine within the local study management as they are the most familiar with the skill level of the programmers being utilized on the study. We also noted that we planned to base the assignments of the Rundo to allow them to gain comfort with Santen's processes and to, at least initially, make assignments based on location to allow all steps to be performed locally. Oversight of the tasks would involve a spreadsheet to note assignments, status, and a central location for questions and comments. Finally, the differences in work schedules were discussed and how we plan to capitalize on easily obtained overlaps while using contingency planning when that isn't possible.

Next we covered the communication category. After determining English would be the common language used, we outlined the need and description of the communication plan that will be created at the start of each project. Weekly global team meetings would be organized to allow timelines, status of task work, and questions to be discussed in an atmosphere we felt would promote the team environment. And the expectation for "same day response" to all communications was explained, even if it was to say a response would be delayed.

The final category of our preplanning focus was process consistency. We detailed three areas we felt that, even though the contract stated Rundo would use Santen's SOPs, needed additional work guidances put into place. The guidances would detail how to program (programming guidance), what to program (display standards), and how to ensure the output was correct (validation process).

As study work is underway using these processes we hope to revisit this topic with a follow-up as to how it all went in a future paper. For now, it is our hope this provides some areas for other teams to take into consideration when constructing their own global team.

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