QUANTEX LABORATORIES

Selection of a CRO is a decision that encompasses many key factors. This paper discusses various points to evaluate when selecting and working with a CRO

Choosing a CRO for Analytical Testing

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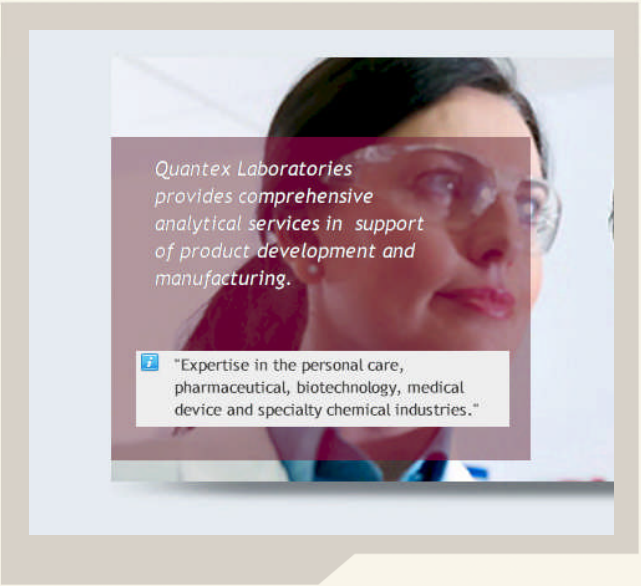

Pharmaceutical companies frequently use contract laboratory organizations (CROs) for all or part of their analytical testing requirements. There are many such CROs, but some are better suited to certain types of projects or to working with particular companies (sponsors).Choosing the wrong CRO can be very costly, therefore companies should consider a number of key factors before making a decision. These include reputation, CGMP compliance, experience, available resources, location, prices, and professional compatibility.

Reputation.

A reputation for high integrity and regulatory compliance is an absolute requirement for any CRO. Where possible, references from inside or outside the sponsor's organization can be indispensable. However, many sponsor confidentiality/non-disclosure agreements (CNDA), which CROs execute, may not allow disclosure or release of information on sponsors and their projects. Consequently, sponsor references may be difficult to obtain. One can also consult independent sources. A good source of independent information about a CRO's reputation are the CRO/CMO industry magazine Life Science Leader, or the market research firm Nice Insights which tracks the CRO space. Life Science Leader and Nice Insights oversee The CRO Leadership Awards. These awards, which receive input for some 40,000 pharma and biotech outsourcing executives, are a good independent confirmation of a CRO's reputation.

CGMP–CGLP compliance

All standard operating procedures (SOPs) must be documented and conform to CGMP–CGLP guidelines. The CRO's SOPs and other relevant work procedures should be reviewed along with any recent regulatory inspection reports. Also, where needed, a facility audit and a meeting with the appropriate CRO staff should be scheduled.

Experience.

Although many CROs routinely perform product release or stability testing, they are not necessarily qualified to perform methods evaluation, development, or validation. These activities require a thorough understanding of analytical chemistry and the ability to design meaningful experiments that help detect and solve non-routine problems. Methods development and validation for highly regulated pharmaceuticals can be completely different from developing test methods for other chemical samples. Experience with specific classes of compounds or dosage forms may be especially valuable.

Laboratory, equipment, and staffing resources.

The antidotal of avoiding overly crowded laboratories is like an "old wife's tale". While there may some truth, it is not a good indicator. One of the largest CRO's has over 100 hplc instruments, stacked literally on top of one another. While to the untrained eye that laboratory

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laboratory appears overly crowded, it in fact is the efficient use of very expensive lab space. Just because a laboratory appears crowed, this in no way reflects adversely on a CRO's capabilities, reputation, experience or ability to carry out your project. A better indicator is that the equipment required for the project is available and has been properly qualified, calibrated, maintained, and documented. An experienced supervisory and laboratory staff is in place and readily accessible to the sponsor, is another indicator. Keep in mind that contact with the CRO staff is important when evaluating the communication between you, the sponsor, and the CRO.

Location.

The CRO's location may be a factor in efficiently conducting a project. Proximity to the sponsor or to an airport may be advantageous for meetings or for delivering samples or special supplies. Video conferencing or other communication systems should be examined for compatibility with the sponsor's equipment. However, given the availability of such services as GoToMeeting, this should not be an issue.

Professional Compatibility.

This relationship characteristic can be difficult to evaluate initially. But becomes very obvious and important after the project has begun. If the sponsor's staff does not work well with that of the CRO, the outcome of a project may not achieve full success. This attribute is difficult to define but is a very real and powerful influence on the daily execution and overall success of a project. Selecting a CRO which historically has taken a collaborative approach with sponsors, is more likely to avoid such difficulties. Particularly if that CRO views themselves as part of the sponsor's staff, only located externally.

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Working Arrangement

Once a selection has been made, the sponsor should provide the CRO with background information regarding its existing products and test methods. The CRO will most likely have a number of questions after review the information provided. At this point the CRO's responsibilities should include evaluating the suitability of any questionable test methods, enhancing existing or developing new methods as well as validating and transferring new methods to the appointed sponsor sites and writing the corresponding documents.

At some point early on in the working arrangement, a decision will have to be made as to how best to employ the CRO's resources. There are at least three different approaches.

The Project Approach

Under this scenario, projects are defined and assigned to the CRO on a project-by-project basis. For relatively small or moderate sized projects, project-by-project pricing and planning can work best because a fair value for the required work can usually be estimated accurately.

Full Time Equivalents (FTE)

In the FTE approach, dedicated full-time CRO staff working at the CRO's site, are specifically working only on behalf of the sponsor and its projects. This approach avoids tying up sponsor resources and takes advantage of the CRO's instrumentation. The physical separation of CRO and sponsor teams can make communication more difficult. However, if a sponsor chooses a CRO which historically has taken a collaborative approach with sponsors, a sponsor is more likely to avoid such difficulties. As with any relationship, sufficient time must be spent building

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trust between the CRO and the sponsor during the initial phases of a project. Keep in mind that to make the best use of the CRO's time and effort, under this arrangement, the sponsor must supply sufficient information, materials, and documentation in a timely fashion.

Professional Staffing

This approach is specifically designed to give the sponsor a "non-permanent" workforce of full-time CRO staff, who are assigned to the sponsor's site. CRO staff hours are usually billed at an agreed-upon rate for a specific period of time, a plan that works very well for large projects. Under this arrangement the CRO hires, trains and manages its staff at the sponsor's site to perform analytical scientific programs using the sponsor's facilities and quality systems. This approach provides a non-permanent way to meet sponsor scientific staffing needs that is fully compliant with co-employment law. And, since the CRO's staff works at the sponsor's facility, it may be managed as the sponsor feels appropriate either by in-house or CRO supervisors. Communication between the sponsor's and contractor's staffs is facilitated through close physical proximity. Moreover, any equipment and systems brought in by the CRO may be closely monitored for compatibility with that of the sponsor's. Key to this approach is that the sponsor can observe how effectively the CRO's staff is working.

Implementing A Contract –Use of a General Master Agreement

Once a CRO has been selected and before any project work is commenced, the sponsor and the CRO should agree about confidentiality; ownership; billing and payment issues; a clear description of all deliverables; the sponsor's responsibilities versus the CRO's responsibilities; communication agreements; equipment and material costs; analysts' sick time, vacation, holidays, overtime, and training; how the project will be managed; how progress will be tracked and communicated; shipping costs; and surplus samples. A general master agreement between the CRO and sponsor may be advantageous. Then, specific project work orders can be submitted containing the details of each project that is included in the general master agreement. Estimating required resources for a non-routine project is difficult because it is hard to predict how much work will be required for each step of the project. Sometimes everything falls into place; at other times, every potential problem that can arise will. The contract should specify how additional work beyond the original scope will be defined, accomplished, and paid for.

The Analytical Team

Once a contract is signed, an analytical team will be assigned to the project. These individuals must possess the skills appropriate for their tasks. Over-skilled individuals may lose interest and end up costing more than necessary. Under-skilled staff may become overwhelmed, make poor decisions, work inefficiently, and even arrive at incorrect conclusions. Often the team is no stronger than the supervisor. Having the right CRO supervisor can make the difference between the success and failure of the overall project. The supervisor must not only understand the project goals and details, possess the appropriate skills, and communicate well with and motivate the CRO staff, but he or she must also be adept at communicating with the sponsor.

Overall plan

Having an written operational plan in place prior to executing the project is absolutely essential. It should be developed jointly by both the sponsor and the CRO. In fact, such a plan is indispensable to complete all project work properly and on schedule. Even the most-skilled analytical team members will not meet the project requirements unless each knows precisely who is responsible for what. Un-communicated assumptions are the enemy and downfall of good intentions and unwritten plans. Some issues to communicate in detail are :

a. What are the final deliverables, including such items as the required format, software, signatures, and so on. It may include all the laboratory work, the draft documents, the issued documents, or the

b. documents once approved by the sponsor. Here, model or example laboratory documents should be shared to help clarify exactly what is needed.

c. What materials and information is required from the sponsor. The plan should clearly document how much of what is needed, when it is needed, and any special requirements related to delivering the product and keeping the project running smoothly.

d. What are the specific responsibilities of the CRO and the sponsor , including responsibility for decision making, problem solving, and reviewing draft and final documents.

e. What are the milestones, timelines, and deadlines. These should be clearly stated in detail.

f. What is the expected quality. This should be defined as clearly as possible, as should be the degree of complexity for the finished product and who will measure and determine whether these expectations have been met.

g. What changes that may be necessary after work has begun or even after completion. Making changes because of lack of forethought or communication can be extremely frustrating and wasteful. Agreed upon cost and timeline changes caused by modifications to the scope of work, process, requirements, and plan should be documented.

The Communication Plan – have one in place at the start

Want to prevent unwanted surprises with a project. A communication plan can help prevent this while at the same time add significant value to a project. As with an endeavor, adequate up-front communication is absolutely vital to success. Rushing into a project before communication lines have been established is a recipe for ineffectiveness, frustration, stress, failure and disaster. It's, therefore, important to make no assumptions and to communicate and thoroughly document agreements. Periodic meetings at regularly scheduled times can help ensure adequate communication. Each meeting should have an agenda and allow time for open discussion. The CRO and sponsor should also agree about the protocol for less-formal communications. Back-up personnel should be assigned to cover the times that to cover the times that the key project personnel are not in the office. Before any emergencies arise, the key personnel may want to make known how they can be contacted outside of work, such as by cell phone or text messaging, and what kind of an emergency would require such communication.

Progress Monitoring

Monitoring the progress of a project can be surprisingly difficult for a complex project and can consume a huge amount of both CRO and sponsor time. Too much time spent on planning and monitoring can be self-defeating because it consumes resources that could be better applied to completing the project. Overly detailed documentation or the need to justify why everything is not exactly on schedule is counter-productive. On the other hand, it is important to monitor progress according to the timeline and budget to ensure that the schedule is met and that costs are within budget. The goal is to strike a balance between monitoring and working toward completion of the project. The CRO and sponsor should discuss and agree up front exactly what should drive the progress of the project if it starts to fall behind schedule. In other words, which factors have priority? Sometimes, as a result of unforeseen problems or inaccurate estimations of the resources required to perform a task, one objective must have priority over another. This distinction should be made as early as possible in the project. Periodically, especially after project completion, project managers should schedule time to review the lessons learned from project experiences. Both the CRO and sponsor should explore and document what worked well and what might be improved in the next project.

This article is based upon a discussion with Dr. Paul Newton of GalaxoSmithKline