IQVIA MEDTECH

White Paper

Outsourcing Clinical Trials for Medical Device Companies

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Executive summary

This paper addresses best practices for medical device and diagnostics clinical trials outsourcing, based on over 20 years of experience leading more than 200 medical device and in vitro diagnostics trials across the globe. IQVIA MedTech considers finding a provider that is aligned not just therapeutically, but also with your technology and culture, to be critical in a successful partnership. Our dedicated device trials team is aligned to your therapy, your technology, and your team.

Whether your organization is a large manufacturer or small new venture, clinical trial outsourcing is a complex process. The complexity of a successful procurement can be managed with good planning and careful selection of the right partner. This paper guides you through a successful contract research organization (CRO) outsourcing process.

As a medical device manufacturer, you and your business leaders are looking for smarter ways to get trials done more efficiently and on budget. Trusting a CRO with your trial can drive results, but also raise risks – will the CRO build positive relationships with my investigators? Are the monitors therapeutically aligned? Can the CRO effectively work with my field engineering and clinical staff? And perhaps most importantly, is the cost-value of partnering the choice for my business? This paper is geared to answer these important questions and help you select the best CRO partner.

This paper is intended to assist medical device and diagnostics manufacturers planning to create better initial partnerships with CROs and expand CRO outsourcing partnerships – whether yours is a new venture or an established manufacturer looking for the best CRO solution in the medical device industry.

CROs and device sponsors go global

Modern medical device and diagnostics sponsors and CROs are increasingly global. In 2019 there are more than 3,000 contract research organizations (CROs) operating worldwide with total combined market revenues exceeding $21 billion, operating 83% of trials in high-income countries.[1] A decade ago, the top 5 CROs employed fewer than 30,000 people, and now there are over 100,000 employees worldwide.

Globalization adds a new aspect to clinical trial outsourcing, with more than 80% of manufacturers executing trials in more than one country, compared to less than half that a decade ago.[2] While the United States remains the largest market for medical devices, in part due to the friendly regulatory environment for novel

MedTech ventures, Asia-Pacific (APAC) is growing by more than 20% each year – making it one of the fastest growing markets in the world.[2]

Selected in 2019 as one of FORTUNE's "World's Most Admired Companies®," IQVIA has feet on the ground in more than 100 countries.[3] This enables us to ensure your medical device trials are executed compliantly and effectively, no matter where in the world your technology is heading.

Mapping the CRO outsourcing pathway: Taking your first steps

A plan is the first thing you need to succeed. First a sponsor should prepare a Request for Information (RFI) and Request for Proposal (RFP). It is common for sponsors to provide a period of time for CROs to ask questions or get clarification on RFP requirements, which may be formal or informal? Questions and answers may be written or discussed live at meetings or teleconferences.

Once the service needs are defined, sponsors can move forward with the outsourcing process, which is divided into several key stages:

1. Request for Information (RFI)
2. Request for Proposal (RFP)
3. Bid Defense, which involves a virtual or onsite meeting with the CRO team
4. CRO selection and award

When the RFP has been put forward, and proposals from CROs start to come in, there are several aspects sponsors should consider before choosing to meet with a prospect for a bid defense:

- Whether the CRO has put forward a therapeutic and technology aligned core team suitable for a medical device trial
- The amount of consideration and expertise the CRO has to ensure the trial is a success
- Alignment of values between that of the sponsor and CRO team
- The CRO longevity and status, including specific previous trial experience
- Whether the CRO has met the requirements set out in the RFP
- The quality of responses to any questions for the CRO provided in the RFP

Based on the CRO responses to the RFP, the sponsor may then plan to conduct an in-person or teleconference meeting called a "bid defense" with one or more CRO providers. It is critical to note that a bid defense cannot get underway without a good proposal. Therefore, it is incumbent on the sponsor seeking a CRO to provide a quality Request for Proposal (RFP) containing as much relevant detail as possible. The ideal RFP should include timelines, draft protocol, project specifications, technical needs (such as EGG or core lab support), assumptions, and any key questions the sponsor has for the CRO. Most sponsors choose to have the field narrowed down to three to five qualified candidates at the RFP stage, and RFP planning is critical to getting the right team and price from your CRO partner.[4,5]

A PRESCRIPTION FOR SUCCESS: PLANNING YOUR OUTSOURCING PROCESS

CROs offer a range of services, up to complete or "full service" outsourcing. Full service outsourcing encompasses the entire trial process, where a range of services are provided by the CRO. Manufacturers sponsoring clinical trials can outsource some or all services. While other models are available, many clinical trials are conducted under full service models. Whether a full service model or only selected services are contracted will depend on your needs as a sponsor.

What is a "full service" clinical trial?

A "full service" trial is one where the manufacturer sponsoring a clinical trial outsources all core clinical operations, and often support and/or lab services as well, to a contract research organization. When determining a clinical trial outsourcing plan, it is possible to outsource some or all services.

CORE CRO SERVICES

- Device/IVD Study Design
- Project Management
- Feasibility & Site Selection
- Investigator & Site Management
- Biostatistics
- Data Management
- Monitoring Solutions
- Medical Affairs & Safety
- Report Writing
- Medical Imaging & Core Lab
- Clinical Regulatory Services

SUPPORT SERVICES

- Predictive & Adaptive Data Solutions
- Adjudication & Safety Boards
- Quality and FDA BIMO Audit Support
- Combination Product Support
- Strategic Regulatory & Commercialization Support

LAB SERVICES

- Central Laboratory Services
- Genomics & Biomarker Solutions
- Imaging Core Lab, Extensive Reader Network
- Cardiovascular Core Lab

"The quality of the RFP can help drive quality CRO bids. Proper planning starts with the RFP. You can also see their [the CRO's] responsiveness and what working with them would be like."

— Executive Survey Respondent

TOP QUESTIONS MEDICAL DEVICE SPONSORS SHOULD ASK IN THE OUTSOURCING PROCESS

As a medical device sponsor, you should start by asking the right questions. We asked industry executives what some of their most common questions for CRO providers were:

GLOBALIZATION 80% of device firms are doing global trials, more than double since 2010 	**DYNAMIC REGULATIONS** drive change, EU MDR & FDA Accelerated 510(k) or direct de novo processes 	**RESEARCH GOING DIGITAL** From genomics to telemedicine, technology has changed the ways clinical trials are done 	**MORE CRO CHOICES** With so many CROs to choose from, finding the right partner is harder than ever 
Do you have staff monitors & operations "feet on the ground" in global regions? In U.S.? EU? APAC?	Is your regulatory staff dedicated to devices?	Do you have a biosensors program?	Do you have therapeutic experts in our area, that focus on businesses like us?
Are you full-service in China?	Is your QMS ISO 14155 compliant, and geared for devices?	Do you have in-house software teams for software as a medical device (SaMD)?	What is your communication strategy, and how highly allocated will my staff be?
Can you help me plan my global strategy?	Do you have a strong record of IDE and CTA expertise in Class IIb & III?	Do you have in-house EDC programmers and core lab / angio lab services?	Do you have engineers and device experts on staff?

AT IQVIA MEDTECH, OUR ANSWER IS YES TO THESE QUESTIONS AND MORE.

STRATEGIC SOURCING AND RELATIONAL OUTSOURCING

Sourcing the right CRO teams is important for medical device sponsors. Several strategic sourcing models have emerged for the CRO landscape. While short-term "fee-for-service" or "time and materials" contracts are suitable for smaller projects, a more sophisticated partnership is necessary to help you run the many aspects of your clinical trials. This is because clinical development often includes many different functional staff, technology solutions, and external (e.g. site and key opinion leader) interactions over a relatively long period of time.

Fee for service: A solution for technical services

For more technical services, a "fee-for-service" (or FFS) structure is deemed most effective where the CRO quotes for a specific scope of work and the sponsor is able to budget with some certainty unless the scope of work materially changes. These services include consulting and regulatory submissions, for instance.

Time and materials: A solution for ongoing projects of limited scope

For services such as statistical or regulatory consulting where the scope of work is relatively flexible and open ended, a "time and materials" contract where the sponsor pays only for actual hours worked at an agreed rate may also be an option.

Unitized services: A solution for daily, weekly, monthly and yearly fees

For activities such as clinical monitoring, a "unitized" (also known as "capitation" because it "caps" daily, weekly or monthly fees) contract structure reflecting items such as costs per full and partial day at site, site management/support (on a site per week or month basis) and clinical quality management (per week or month) are often regarded as the most appropriate contracting and budgeting mechanisms. For the providers this structure guarantees that the agreed amount will be received, while providing sponsors clarity.

The preceding three structures are common pricing arrangements for CROs. However, for large projects like clinical trials, services using a time and materials costing model put all the risk on the sponsor, and do not provide incentives for efficiency and lean CRO practices that save money.

Preferred and partnership models

A preferred model is a relational model that is based on risk and reward. There are three types of relational models to consider, including the preferred provider model, performance-based model, and vested business model.

These models enable medical device sponsors to establish long-term relationships with the CRO partner, which add value over the life of clinical development projects.

Generally speaking, small CROs typically do not have sufficient staff or experience for lifecycle partnerships in medical devices, which require engagement in strategic regulatory planning, design development and quality, clinical trials, commercialization services, and strategic data solutions. This is where a full scope CRO provider can add long-term value.

Strategic sourcing & procurement models

CRO partnerships may be designed in several ways to add value for the sponsor.

PERFORMANCE BASED MODELS

Performance based models use Key Performance Indicators (KPIs).

Value can be achieved for milestones, such as regulatory submissions or clinical trial goals (e.g. activating sites, first-patient-in, all patients completed for primary endpoints). This model requires a higher degree of integration and collaboration between the sponsor and CRO partner.

Because milestones are clearly provided, sponsors and CROs working towards aligned objectives with clear goals. KPIs must be clearly defined and realistic in order to ensure the partnership success.

VESTED DEVELOPMENT MODEL

Vested development models involve the CRO early in actual product and clinical development.

This model rewards performance and novel ideas the CRO brings to the table. Key operations and scientific staff thus may be involved from development (e.g. product documents and protocols) to execution. This streamlines project issues and prevents downstream issues.

A vested development model is a collaborative business model that drives relationships. This model often begins with early engagements in the clinical development process where the CRO is rewarded for value-add contributions, setting the stage for innovations.

PREFERRED PARTNER MODEL

Preferred providers are vendors that have priority status for awardable projects.

In this model, CROs attain repeat business and sponsors save time, energy and costs in qualifying vendors and bundling services. Because there is long-term repeat business, the preferred provider can often tailor or expand services for preferred clients.

Generally, preferred providers must have comprehensive service offerings for bundling to be effective, which are not typically available at small and mid-sized CROs. Preferred Provider Partnerships streamline revenues and execution of clinical programs.

GETTING STARTED: HOW TO CONSTRUCT AN INITIAL REQUEST FOR INFORMATION (RFI)

The Request for Information (RFI) process is designed to gain information about potential outsourcing partners (CROs) and determine if each organization has the qualifications to be included in a more formal and comprehensive RFP.

There are two critical parts to a successful RFI:

1. Determine which CROs should receive the request. Medical device sponsors have numerous resources from which to develop a list of CROs to be included in the RFI process. Seek recommendations of staff and industry contacts with outsourcing or CRO experience. Attend industry conferences such as the annual AdvaMed MedTech, Euromeeting, Medical Device Forum, or therapeutically aligned meetings, such as EuroPCR (European Society of Cardiology) in cardiovascular. Conduct independent research through industry journals and online resources. Look for specific medical device and diagnostics experience and in-house data solutions – beware of CROs who claim device experience without a dedicated division and staff for devices.

   Please note: Prior to providing any confidential information like that included in an RFI, sponsors should solicit and execute a non-disclosure agreement (NDA) with the CRO, also known as a confidentiality agreement (CA), confidential disclosure agreement (CDA), or proprietary information agreement (PIA) in some regions.

2. Determine what information is needed from each. The detail with which RFIs are written varies widely. As a starting point, a base level RFI table follows.

Table 1. Key Components of a Request for Information (RFI)

CRO CORPORATE OVERVIEW	History, ownership, financial summary, geographic locations and experience, suite of services, functional support, executive and management staff, organizational chart, governance model
MEDICAL DEVICE EXPERIENCE OVERVIEW	Departmental overview, history, key staff, experience in your class of device
TECHNOLOGY EXPERIENCE	Key technologies (e.g. core lab, imaging, laboratory assays, software, hardware, etc.)
THERAPEUTIC EXPERIENCE	Indication and organ class
SUBMISSIONS EXPERIENCE	510(k), IDE PMA, CE Mark, etc.
TRIAL TYPE EXPERIENCE	Specific medical device premarket (first-in-human pilots, feasibility, pivotal) and post-market trials.* Geography, scope of work, regulatory and development position number of sites, scope, sample size
QUALITY	Overview of quality management system and processes, audit history, ISO 14155 QMS compliance, SOPs
STAFF TRAINING AND CONTINUING EDUCATION	Requirements for ICH / ISO 14155 GCP, MDD and CFR 803, 812 regulations (as applicable)
PRECLINICAL, REGULATORY AND REIMBURSEMENT EXPERTISE (OPTIONAL)	Services and expertise, including with the new FDA-CMS (Center for Medicare and Medicaid Reimbursement in the U.S.)
REFERENCES	Current and former client references

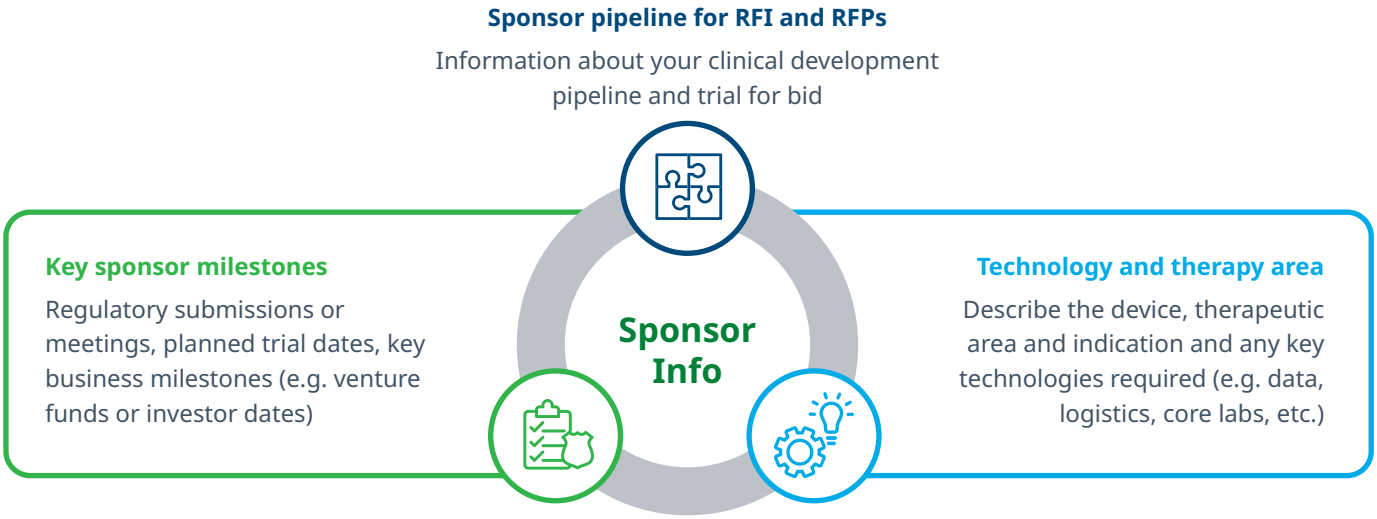
*Note that trials for medical devices, unlike drug trials, are not classified by "phases I-IV" but rather by several categories (first-in-human/early feasibility pilot, traditional feasibility trial, pivotal trial, and post-market or post-approval trials).

Sponsors should include a brief background on the organization's pipeline, technology, and key goals or milestones. Clear instructions on completing the RFI and the submission process will speed responses. The more information provided about the outsourcing need, the more tailored the responses will be to sponsor needs.

CROs should typically be given about two weeks to complete the RFI.

The RFI and RFP are designed to help CRO teams get to know your team – and their specific needs

Sponsors will work closely with their CRO partners, over months or even years. The RFI and RFP should help the CRO team get to know your goals, team, and technology.



Based on the RFI responses, the sponsor should now be able to create a short list of CROs to move to the next phase – the RFP. The next section of this paper focuses on providing detailed information for the RFP process.

THE RFP "STANDARD OF CARE": CREATING A WELL-CRAFTED REQUEST FOR PROPOSAL

Just like in standards of care in medicine, there are standard processes that most CROs and sponsors follow to generate Requests for Proposals (RFP) that drive results. These best practices can help you get best results in the CRO selection process.

With the goal of receiving uniform and consistent proposals across the various CROs, creating an efficient RFP process begins with a thoughtfully crafted proposal document. This document serves as the roadmap for the clinical trial bidding process and guides the selected CROs in how to both develop a strategic approach and create an accurate budget to complete the project.

When developing an RFP, sponsors should be very clear in defining services required and ensure specifications are explicit and consistent across all requested areas of service.

An alternate approach may be to ask the CRO to develop some of the requisite specifications as a way of gaining some insight to (and benefit from) their expertise. However, this approach will create variability among budgets and may make analysis of the different budgets more difficult. This can be avoided by asking for two scenarios: one to obtain an equal-specification budget and another for the CRO's strategic view on the study.

Sponsors should include the following critical information in the RFP document:

Table 2. Key components of a Request for Information (RFI)

TYPE OF DEVICE STUDY	First-in-human/early feasibility pilot, traditional feasibility, pivotal, post-market (including special types of post-market trials for regulatory use, such as post-approval or post-market clinical follow-up trials)
RISK DETERMINATION / IDE REQUIREMENTS	For U.S. studies, significant risk (IDE required), Non-significant Risk, IDE Exempt; EU Classification per MDR/IVDR; Risk status in other global regions (e.g. Japan Shonin, etc.)*
KEY DATES AND MILESTONES	• Device availability timelines, e.g. when device will be available when contract manufacturing organization (CMO)/importer is used • Agency meetings or regulatory filings planned • First subject in (FSI) • Last subject in (LSI) • Last subject out (LSO) • Long term follow-up dates • Key regulatory filing and/or marketing application target dates (e.g. PMA/HDE, 510(k), de novo, or CE Mark filing dates planned) • Final CSR deliverable and any interim data results
COMMERCIALIZATION & REIMBURSEMENT ROUTES	Which countries are targeted for commercialization/payer coverage (e.g. FDA approval/ clearance, EU CE Mark, China NMPA Registration, Japan Shonin, etc.). For FDA, will CMS/HTA review occur**
ENDPOINTS / DATA MEASURES	• Primary and secondary trial endpoints • Health economics and outcomes research • Patient reported outcomes (PRO/ePro) • Workflow data
NUMBER OF SITES AND COUNTRIES	Number and location of clinical site(s)
LOCATIONS OF OTHER KEY SITES/SERVICES	Number and location of site(s) and important services (e.g. depots, readers/evaluators, core labs), where applicable
ESTIMATED SAMPLE SIZE, INCLUDING LOSS/ATTRITION	Target sample size for analysis (N) and total for enrollment, considering those that will not qualify to participate (screen failures) and attrition (dropouts and loss due to death or deterioration are particularly important to consider in invasive studies with long-term follow-up periods)

PROCEDURES	Total unique clinical procedures/interventions performed
SCOPE OF DATA COLLECTED (CASE REPORT FORMS, "CRF/eCRF")	Typically the number of "pages" required for a protocol, unique and repeat (e.g. used at multiple visits). Any requirements for medical coding or standards (e.g. CDISC).
DATA OUTPUTS	Estimate of tables, listings, figures to be outputted as part of the studies statistical results. For device trials, these should include at minimum primary measures and safety listing (e.g. AE/SAE/UADE and device defects)
OUTSOURCED SERVICES	Responsibilities outsourced to CRO vs those retained by the sponsor *(see overview of CRO services earlier in this document)*
SAFETY EVENTS	Expected number of adverse events, serious adverse events, and unanticipated adverse device events (AEs/SAEs/UADEs), which should match the study risk level and be informed by prior device trial experience
MONITORING	Number, frequency and duration of monitoring visits, and if "risk-based" monitoring is required
OTHER DATA SERVICES NEEDED	Other data, such as: • Electronic informed consent services (eConsent) • ECG/EEG waveforms • DICOM imaging and core lab • Angiography lab or cath lab data • Collection of RAW, telemedicine, or device-level data in Software as a Medical Device (SaMD) and Clinical Decision Support (CDS) products • Other data requirements

*Note that trials for medical devices, unlike drug trials, are not classified by "phases 1-4" but rather by several categories (first-in-human/early feasibility pilot, traditional feasibility trial, pivotal trial, and post-market or post-approval trials).

** The United States (U.S.) Food and Drug Administration (FDA) and Center for Medicare and Medicaid Services (CMS) that regulate public payor coverage in the U.S. now offer a parallel review program that enables device manufacturers to seek feedback on the payor coverage requirements while still in the pre-market environment, even before their clinical trials begin[6]

Upon receipt of the RFP, sponsors should expect a round of questions from the bidding CROs. Questions are typically compiled as questions and answers within one document (or Excel sheet) and provided to each to ensure the distribution of uniform information. Sponsors should also evaluate the quality of questions to evaluate each CRO's understanding of the space.

Anatomy of proposals: budget drivers and review

Sponsors should consider supplying a budget spreadsheet to each CRO to complete as opposed to each submitting a budget in disparate formats. The spreadsheet should include number of units, positions and hours assumed per task. Be cautioned, however: each CRO uses unique internal tools that may be mapped into the spreadsheet differently – some variations are to be expected and are not indicative of flaws with the process. It is also helpful to review budgets at a more macro level (e.g., cost per patient) to ensure the detailed tasks add up to a common-sense level of resources and investment.

BUDGET TYPES AND BUDGET DRIVERS

Sponsors typically dictate the type of budget they prefer: unitized, time and materials, fee-for-service, etc. As discussed earlier in this paper, establishing preferred partnership may increase the value-add and drive goal alignment between sponsor and CRO.

It is also helpful to understand the primary cost drivers for CRO tasks. Some drivers of the larger cost items include:

- Clinical monitoring activities and the associated resource and cost levels will depend upon site numbers, country/location distribution, patient/data volume per site, and length of the study.
- Regulatory and site startup timelines and resource levels will be driven by the extent to which the CRO is supporting strategic discussions with the relevant authorities, the countries involved, and the type of sites and IRB/Ethics committees involved in the study. Additionally the startup process usually requires significant sponsor/CRO teamwork to establish site contracts, budgets, etc. in an efficient manner. This area can have a substantial impact on budget and timelines if not properly outlined and managed.
- Data management and electronic data capture (EDC) costs will be driven primarily by the complexity of the CRF and associated edit checks, page/data volumes, and variables such as data import/export volumes, and analysis numbers.
- Statistical review is primarily driven by the complexity of the analysis, number of interim analyses and the total number of deliverables (e.g., TLFs) expected over the life of the study.
- Overall project management fees are driven by the geographical breadth of the study, the number of services being outsourced (more services equal more integration to manage), the number of external parties to manage, and the overall study duration.
- Data solutions such as electronic informed consent (eConsent), electronic capture of patient reported outcomes measures (ePRO), risk-based monitoring (RBM), image and RAW file services (core lab services) may add costs for small studies, but can add value over time by improving study efficiency and sponsor access to data in real or near real time.

DIAGNOSING THE RESPONSES: HOW TO ASSESS CRO PROPOSALS

Once the RFP responses have been received, sponsors need a formal evaluation process. This may include the development of an evaluation worksheet for each team member to use as they review RFP responses. This document should highlight areas of importance to the sponsor and include a scoring system and definition of each score.

Most importantly, the sponsor team should consider the CRO team, the people that they will be collaborating with over the next month and years after the trial is awarded.

Both “hard” criteria (e.g., therapeutic experience, geography, quality systems, allocation of appropriate staff, etc.) and “soft” criteria (e.g. cultural fit, team fit, personalities, scientific and creative ability of the core staff) should be considered as important measures in sponsor decisions to outsource to a CRO.

People are the heart of collaboration in clinical teams. Choose the right CRO partner to support your sponsor team.

Managing a budget review

Many sponsors begin the RFP review process at the budget summary. Wide variances in bids (>40%) indicate the assumptions and/or services included may vary from bid to bid, and should result in a clarification of assumptions from the sponsor and an opportunity for each CRO to adjust its bid. This information will be fairly easy to determine if the sponsor has supplied the aforementioned budget spreadsheet.

Moderate variances in price (20-30%) are to be expected and should be viewed not as exclusionary criteria but rather a starting point of evaluation (see more on budgets below).

Summary budgets also provide excellent fodder for questions and answers to be conducted during bid defense meetings. Noting where each CRO identifies a need for time and resources based on the study design demonstrates an understanding (or lack thereof) of the trial process, nuances of medical device and diagnostics trials (as opposed to drug studies), technology efficiencies and historical knowledge of similar trials and should be viewed and questioned accordingly.

Text review

Text review typically follows. Sponsors should read RFP response text for thoughtful language customized to the specific trial – not boilerplate language included in every RFP response. Key indicators include:

- Insights regarding the therapy and study intents
- Guidance or comments on regulatory strategy/path
- Protocol comments and/or challenges

- Identification of risks (e.g., enrollment, procedural adoption, site relationship and previous history)
- Data or commentary on feasibility (if requested)

Also look for the CRO to demonstrate knowledge in areas like serious/unanticipated adverse events reporting requirements, forms required for site startup, reimbursement strategies, etc. These are all areas in which an inexperienced CRO may show naivety.

Study staffing

Another key evaluation point is proposed study staff. Medical device companies need to be especially vigilant about delving into the backgrounds of proposed staff that may either be generally inexperienced or come from exclusively pharmaceutical trial backgrounds. Ask for full CVs (not abridged biographies) of each proposed team member. Inquire about both therapeutic experience and device type; and for CROs who make the short list for a bid defense, request the proposed project manager attend the bid defense in person.

If the proposed project team appears qualified, sponsors should also inquire about the following:

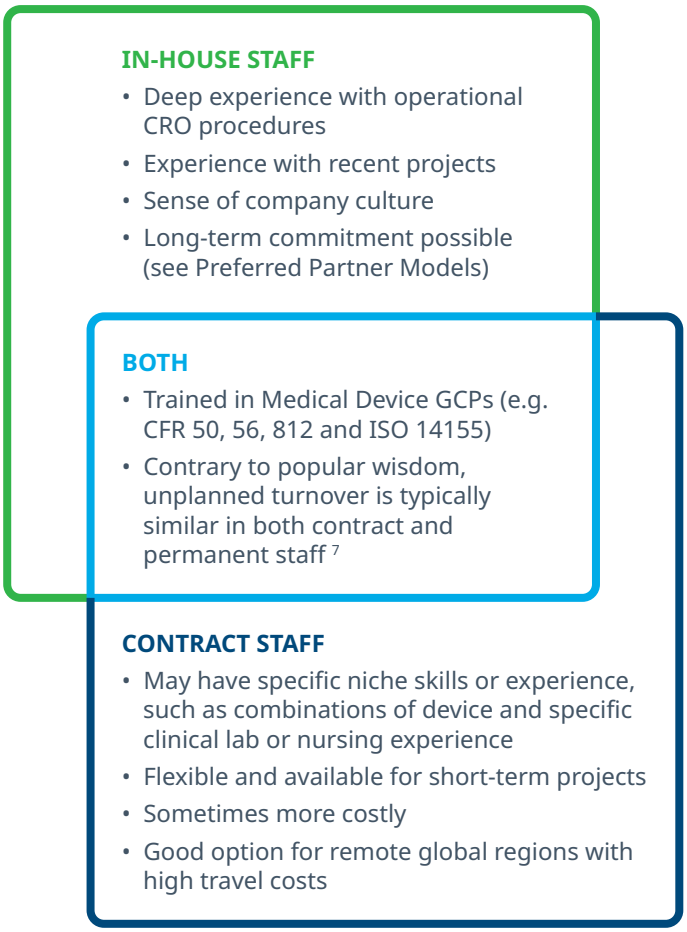
- How much of their time is available to dedicate to this study and when will that time be available? Alternatively, what are the chances this team will not be available at the time my study is scheduled to begin, and what is the CRO's alternative staffing plan?

- Do core team members have device engineering and clinical expense (not just drug) experience?
- Where are the proposed team members located?
- How is the project team managed? Are line managers used?

Sponsors should also be aware of CRO staffing models – is the proposed team comprised of employees or contractors? Pros and cons follow for each.

Permanent or contract staff – Which is better?

Experienced and device-focused staff are essential to your projects. Hybrid permanent-contract staff projects are the most common in modern CROs. While small CROs often have a limited pool of in-house staff, larger CROs can provide both permanent in-house staff and leverage sourcing for ideal contractors for temporary or highly specific assignments.



Reference calls

It is a good practice to ask for references during the RFP stage, even if calls are not placed until after the bid defense has taken place. However, any CRO can provide good references. Tailor your request to references currently working with the CRO as well as a former client(s). Ask the CRO to include references that have similar devices or therapeutic areas, or a similar trial design. And when reference calls are placed, ask questions around hot button issues for your organization. Was the CRO easy to work with? Was the project manager a leader who made his or her job easier? How did the CRO deal with challenges? Was the budget managed properly and proactively? Were the sites pleased with their work? Does the CRO have a track record of ISO 14155 and 21 CFR 812 compliance for medical devices?

Budget evaluation

As previously noted, budgets should not be viewed in isolation or as exclusionary criteria. Additionally, the old adage of excluding the least expensive and the most expensive should not be followed in this case. Rather, pricing should be viewed as a topic for exploration, with many CROs willing to work with sponsors to come to a mutually agreed upon cost, structure and scope. CROs interested in true partnerships will demonstrate transparency in pricing and provide details upon request that go beyond the budget worksheet.

CROs typically require 10-15% of direct costs be provided upon the execution of the contract, but this varies depending on the size and nature of the study. If the sponsor organization has a rich pipeline, inquire about Preferred Provider status and volume discounts (assuming the CRO is a good fit across all studies).

Sponsors may also request the CRO metrics around changes in scope. CROs may price low but ultimately cost more than a competitor by initiating multiple and pricey contract amendments. This is not only a headache for the sponsor, but can create financial challenges as well. True changes in scope should be sponsor-initiated

and reflect new circumstances around the trial (not an estimation error on behalf of the CRO). Regular budget review meetings between sponsors and the CRO help manage and identify budget issues and allow for proactive resolution avoiding costly changes in scope.

THE GOLD STANDARD OF CRO SELECTION: MAKING THE MOST OF CRO BID DEFENSE MEETINGS

Once the sponsor has reviewed the RFP responses, the final step is choosing CROs to be included to proceed to the next step, where the sponsor meets with the core team and business leaders from the CRO that are assigned to the project.

These meetings between sponsor and CRO teams to evaluate a CRO proposal are called "bid defense" meetings. These meetings may be conducted remotely by teleconference or phone but are most commonly conducted in person for large medical device trial projects. This allows the teams to meet, and sponsors can assess both technical strengths of the CRO proposal as well as softer metrics, like cultural fit and team engagement.

Bid defense meetings, typically conducted in person, have been traditionally considered the gold standard in the selection process. By meeting with the team in person for several hours, sponsors are given peace of mind as they prepare to make a final decision on which CRO partner they will choose, a commitment that may mean months or years of collaboration between teams. Notably, modern medical device sponsors can choose the bid defense, or other less formal processes, to finalize their selection.

When a medical device sponsor wants to move forward with a conventional bid defense meeting, the sponsor should notify the CRO in writing (typically via email) that the CRO team is invited to bid defense meeting. The sponsor usually suggests a selection of proposed dates and times and leaves the rest to the CRO.

To get the most out of your bid defense meeting, whether conventional in-person meeting or teleconference, we suggest that sponsors:

- Clearly outline for each CRO what you expect to learn during the bid defense including any gray areas from the RFP responses.
- Request the proposed project manager attend – and try to spend time with that person beyond the formal meeting to assess confidence and chemistry.
- Ask to see sample clinical trial management system (CTMS) reports or demos, and fully understand the CRO data and reporting capabilities. Evaluate whether the CTMS and the related reports provide the desired level of transparency. Also consider that a lack of a detailed CTMS and electronic trial master file (eTMF) system may indicate an immature infrastructure within the CRO.
- Explore knowledge of and potential relationships with key opinion leaders (KOLs) in the relevant therapeutic area. Probe to determine the extent of knowledge/relationships. (While existing relationships are not critical, they can be very helpful in propelling the study through the startup phase as well as providing guidance.)
- Inquire about medical device specific quality management systems, including compliance with ISO 141155 and EU MDR and well as 21 CFR 812 requirements specific to medical devices, and request the CRO's audit history including results of FDA/MHRA and Notified Body (NB) inspections.

Do not underestimate the importance of team chemistry. Keep in mind that while having a wonderful rapport with the CRO's business development representative is nice, once the project is awarded his or her role will be limited. Take the time to focus on the project manager and the senior executive assigned to the study, and evaluate how well those individuals will mesh with the sponsor team.

Your people are the heart of your product, and nothing affects your staff more than the people they work with each day. You may work with a CRO partner for months, or even years, on your clinical trials and beyond. That is why choosing the right partner and the right model are essential to a successful partnership.

Many sponsors find a clear frontrunner after the bid defense meetings are complete. Experience, project team, chemistry, quality and geography all play a role in determining the best fit for the trial. Revisit the initial criteria deemed to be most important to align decision makers and make a final choice. Alert the CROs in a timely manner and provide feedback (if requested) to each team so they can learn from the bid process.

SPECIAL CONSIDERATIONS FOR IVD BUDGETS AND BID DEFENSES

In vitro diagnostics (IVDs) are unique from other medical devices and have special requirements. We suggest you ask your CRO provider about their understanding of the intricacies of IVD studies including specifically, how operational and pricing flexibility are considered and implemented in regard to core services for IVD studies. Of note, consider inviting certain key team members to bid defenses and that the CRO counterpart be present to ensure alignment. Our recommendations include:

- Does your CRO use internal/external central labs? How are these labs qualified if they are partner labs and what if any are the labs' limitations for large specimen collection studies, instrumentation, etc.? What is the biorepository capacity/ limitations?
- Does the CRO have experience working with leading and emerging IVD & Life Science CDx leaders, IVD manufacturers, and/or pharmaceutical leaders with CDx programs? How is this experience applied and tailored by your CROs project teams and leadership?
- How does your CRO ensure seamless integration between laboratory data and clinical EDC platforms, and how adaptable is your CRO to managing the integration of multiple outputs including sponsor systems?
- Can the CRO team work with / provide specimen collection kits? Is this a service that is provided internally or do you use preferred vendors?
- Does the CRO have the service capacity include in-house global anatomic pathologists who have been trained and proficient to report out often complex results?

- Does the CRO have in-house genomics sequencing, including software teams?
- Does the CRO have Clinical Laboratory Improvement Amendments (CLIA) filing experience, including 510(k)-CLIA dual submission?
- Have you submitted PMAs for IVDs to the U.S. FDA?
- Does the CRO have a plan for IVDR compliance?
- Can the CRO provide an end-to-end strategic solution for the complete product lifecycle, concept to clinical trial, and to market?
- Does the CRO specifically have medical device and diagnostic sites globally, with an established relationship with centers that have demonstrated success and strong track records of compliance research?

DATA IS THE LIFEBLOOD OF RESEARCH – CAN YOUR CRO MANAGE IT?

In today's modern medical device and diagnostics landscape, data has become increasingly important. From digital health products, to mobile health, biosensors and gene sequencing, data plays an increasingly important role in both clinical trials and health care. While most modern CROs have access to electronic data capture systems (EDC) with electronic case report forms (eCRF), don't forget to ask your CRO partner about their data infrastructure and solutions, including:

- Is the CRO experienced in working with other major data services providers, such as those that make EDC systems?
- What data will be available to the sponsor in real time, and what data must flow through manual processes?
- Does the CRO use software and/or gateways to manage safety reporting and regulatory submissions?
- Does the CRO team have experience working with data, such as EEG/ECK waveforms, diagnostic imaging (DICOM), photographic images (such as microscopy or surgical/dermatological images)?
- Can the CRO work with biosensors, electronic medical records (EMR), and medical picture archiving and communication systems (PACs) common at clinical research sites?
- Does the CRO have in-house information technology (IT) and software data solutions?

The right solution involves both data and people. IQVIA offers an unparalleled full-service solution in human data science for clinical research.

Conclusions

Clinical trial outsourcing on behalf of medical device and diagnostics sponsors can provide tremendous benefits including efficiencies in time, human resources and capital. Mutually beneficial relationships between CROs and sponsors yield rewards to both entities as well as patients awaiting new and innovative therapies. Understanding the process and nuances of choosing the CRO for a specific trial will serve sponsors well throughout the life of the study. IQVIA MedTech is here to help both emerging and established medical device and diagnostics firms develop ideal CRO outsourcing solutions and preferred partnerships for clinical research.

Up to 30% faster startup feasibility science enabled by the IQVIA CORE™

Increased site compliance and reduced deviations

Experts in site startup and CTA/IDE filing

Value-add monitoring geared for working with ISO 14155 device trials

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About IQVIA™ MedTech

IQVIA™ MedTech, part of IQVIA (NYSE:IQV), is dedicated to supporting the needs of the Medical Device and In Vitro Diagnostics industry, focusing on the orchestration of "concept to market" business processes to improve patient care. IQVIA MedTech Solutions are powered by the IQVIA CORE™, delivering unique and actionable insights and execution capabilities at the intersection extensive domain expertise, transformative technology, and large-scale analytics. IQVIA is a leading global provider of information, innovative technology solutions, and contract research services. Learn more at iqviamedtech.com.

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