BY DENISE MYSHKO

Creating EFFECTIVE OUTSOURCING PARTNERSHIPS

Pharmaceutical companies are *adopting a more strategic approach* to outsourcing clinical-research services.

CONTRACT RESEARCH OUTSOURCING has grown exponentially over the past 30 years. In the 1970s, outsourcing was limited to pre-clinical and clinical-trial services, according to a report by Kalorama Information. Today, this is a full-service industry that covers the entire drug-development process.

Pharmaceutical companies turn to drug-development service partners not only to take on tasks the companies cannot perform in-house, but also to boost the skill base, keep down costs, and reduce drug-development timelines.

In 2004, it is estimated that almost 42% of all pharmaceutical drug-

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development expenditures will be committed to outsourcing, compared with 4% in the early 1990s, according to the Kalorama report.

This year, the contract research outsourcing market is expected to reach $15.8 billion. Kalorama researchers predict that the amount of R&D spending headed out of house to research suppliers engaged in drug development will grow 14% annually for the next few years, to reach about $28 billion in 2008. The compound annual growth rate forecast for outsourced spending in the coming years is almost double the anticipated increase in R&D spending generally.

The new study, Outsourcing in Drug Development: The Contract Research Market from Preclinical to Phase III, found that the established contract research organizations, or CROs, stand to gain the most from these spending increases, but that there are a variety of smaller organizations that also are poised to reap the rewards.

Analysis from Frost & Sullivan reveals that this industry sector generated revenue totaling $7.78 billion in 2002. Total market revenue is expected to reach $14.37 billion in 2007.

> Pharma companies should hire the best service organizations they can, but that is not necessarily the largest company. Current selection processes that focus on size and range of services may mean that the most qualified, but smaller, partners are overlooked.
>
> *JOHN HUDAK*

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I'm always amazed at the relatively large amounts of money that sponsors invest in outsourcing and how they manage that investment. A number of companies have taken the time to understand how to better outsource by taking a scientific approach.

JOSEF H. VON RICKENBACH

More and more, pharmaceutical companies want to deal with CROs that offer a vast array of services. They want to deal with CROs and other vendors that are more similar to them in terms of being full service and having global research.

LLOYD BARODDY

Globalization is here and here to stay, so I would advise any CRO to get a global partner. Any CRO that is based in the United States needs to have a partner in Eastern Europe, Western Europe, and Asia for studies.

MARK LANFEAR

The Outsourcing Relationship

ZABROWSKI. The key word here is partner. Historically at Roche we viewed CROs as companies that were there to help us with the overflow in a one-off type opportunity. In the last two years, we've changed our thinking about our relationships with CROs. We believe there is value in developing long-term partnerships with one or two of the multinational CROs. For example, timelines and the cost of clinical trials can be reduced if there is continuity between the two companies so that they understand each other and are able to work together to deliver the services that are required. It's also important to have continuity for the people who work on the teams as this strengthens the working relationship. By understanding each other's processes and culture, we believe that also will improve efficiencies.

BALIAN. Industry is evaluating the entire approach to outsourcing in terms of the development process. We're looking for partners to take accountability as if the project were their own and deliver the high-quality, high-standard data that are needed to get drugs approved.

HIGGINBOTHAM. Pharmaceutical companies are adopting a more strategic approach to outsourcing. One of the big drivers of that trend is that outsourcing is a more capital-efficient alternative to expanding a company's infrastructure. In terms of the growth of CROs, that means an increased penetration of the amount of work they are doing with their pharmaceutical customers. There also are new players coming into the market; smaller emerging pharmaceutical companies and the biotech sector are increasingly turning to CROs to access expertise and infrastructure.

LANFEAR. Bigger pharmaceutical companies want to align themselves with three or four CROs. Because the contracting process is so long, these companies need efficiency so they want to choose a partner from an identified few. In addition, pharma companies are running trials globally, so they need a CRO that has that reach. Sponsors may compromise consistency and quality to have that global scope. With the electronic age and with smaller CROs starting to align themselves with each other, a small CRO can more easily do studies for sponsors globally. It isn't always necessary for this type of work to turn to giant, publicly held CROs that may have some of the same issues as large, publicly traded pharmaceutical companies.

VON RICKENBACH. Pharma companies, especially smaller companies, prefer to use a one-stop shop. Maintaining these relationships is expensive and not necessarily integrated. Pharma decision makers want to connect with one person who can quickly provide the com-

We want to share in our customers' clinical-development goals. The earlier we get involved in that process, the more value we can add.

SIMON HIGGINBOTHAM

pany with whatever their company requires. Efficiencies are identified in working this way.

ZABROWSKI. We're still in the process of finding our partners. To do this, we developed a set of questions, which outline the capabilities we're interested in. We then follow up with discussions between the technical experts and the discipline experts in both organizations so that we can understand each other's internal processes, as well as the qualitative aspects, such as the chemistry of the people who would be working together. We also want to determine if the CROs are aligned with our vision of how we view drug development going forward.

ANDREWS. At MedImmune, we outsource a large majority of work, and we do have partners in the true sense of the word. That is a word I never really believed before. In the spirit of the partnership, the core management team from the CRO and MedImmune meet every three weeks to discuss issues and status. As a further commitment to the relationship from our CRO, they have provided us with a director for each of our therapeutic areas who is dedicated to our needs.

LANFEAR. The future trends in outsourcing are going to be that pharmaceutical companies

For the last two to three years, we've paid a huge amount of attention to retention. We've put a lot of energy into looking at what it is people need in order to stay happily engaged.

JULIE MACMILLAN

If a company is looking for quality and timeliness, then there has to be a reasonableness on the cost side. On the other hand, if the only driver is cost, then they must expect to compromise on quality.

DR. KENNETH BOROW

will begin to make strategic long-term alliances and they will do this in the areas that are outside their expertise. This will occur in monitoring and data management as well. We may even see some regulatory tasks being handed off, and pharmaceutical companies will focus on their core competencies — developing drugs.

LANGIN. It's a lot easier for a small-to-midsize

pharmaceutical/biotechnology company to make a decision versus some of the larger organizations where the decisions are being made by contract departments. Historically a large pharma company has a committee or subcommittee that makes the decision about where to outsource, and these committees tend to work with the large global CROs.

MITCHEL. Integrating multinational studies is a challenge for the CRO. My bias is to regionalize. Within given areas, CROs need to have people accountable and responsible for the project within a given geographic area instead of a central area of responsibility. Each group is semi-autonomous. This structure, though, has to respect cultural differences. In spite of standardization, there are cultural issues companies have to address.

ZABROWSKI. The quality of the data generated is the highest priority. If there are questions about a company being able to deliver quality data, that would immediately discount them. Or, if a CRO didn't have certain capabilities, for example if it wasn't truly global, that CRO would also be discounted. And lastly, it comes back to chemistry. If, in our discussions, we just don't feel that we're aligned in meeting the objectives of our partnership and that we wouldn't be able to develop a sustainable long-term relationship, that would play a key part in the decision making.

ANDREWS. Cost is obviously a factor I consider when looking for a contract research partner, but it is never my top criteria. What I look at first with a CRO is the senior-level management. I want to make sure that they are going to remain dedicated to the project after the contract is awarded and signed. I like to have quarterly meetings with a member of the company's senior management. Typically,

Many pharma companies are out-tasking rather than outsourcing. They leave projects to the last minute and then there are certain tasks they can't manage in-house. I would recommend strategic outsourcing rather than out-tasking.

BILL TAAFFE

I don't want to limit the number of vendors or limit them for a duration of time, but I do want to build special relationships with my partners.

JOHN BALIAN

when outsourcing doesn't go well, sponsors only call CROs into the office when they are ready to fire them. I want to be able to share with them what's going well and what we could be doing better on a routine basis to avoid being reactive. No matter how good a project team is, those team members are usually not in a position to get additional resources if they need them. I want to see senior-management involvement; I want the buck to stop at the top.

ZABROWSKI. Quality is non-negotiable. Between speed and cost, I think most people would agree speed is most important. When CROs market their companies and they talk about saving a million dollars in a clinical trial, my question to them will always be: "But when did you finish that trial in relation to the agreed-upon plan?" Prioritization between speed and cost needs to be understood. It is not realistic to think that a CRO will break recruitment speed records while pharma is trying to squeeze their margins to the lowest possible percentage. The CROs must make an acceptable profit to be willing to enter into this type of partnership. In fact, we are trying to take the cost discussion out of the project team and let the business development people negotiate the cost. This makes the process better because it allows the teams to focus on the quality of the data and project plan.

LANGIN. The old adage that you get what you pay for is true here. When pharma companies have three or four CROs giving bids, the budgets can vary. In the past, sponsors would take the lowest bid because they believed CROs all did the same thing. But they found out they didn't always get the same results and were then forced to correct the mistakes made. There wasn't an apples-to-apples comparison done during their exhaustive evaluation process. Price is a sensitive issue here. Quality is the greater issue.

BALIAN. Pharma companies are not getting what they expect from CROs but that is not just the fault of the suppliers. The fault is mutual. Pharmaceutical companies don't outline clearly what they are looking for in advance, and they don't get agreement in advance on the specifics. There are misunderstandings or misinterpretations of the task-ownership matrix. Changes become inevitable and the supplier is blamed. Occasionally, the supplier doesn't present a realistic scenario and after initiating the work, the delivery was not on time or the quality was not what was promised.

LANFEAR. I would say that only 20% to 30% of the time pharma companies get what they expect. One of the reasons is that the language that CROs use is different from what pharma personnel use. The two groups are not communicating properly. That's why we haven't seen good, strong strategic alliances that last. The CROs look at things on a cost-perspective basis because they're in such competition with each other. CROs believe that pharmaceutical companies are concerned solely with cost. So CROs reduce their costs, which makes the pharma companies happy at first. In the end, the price they are charging is not enough to deliver their services with the highest quality to meet sponsor expectations and regulatory compliance. Partnerships need to be built beyond the contract-task level; partnerships should be based on a consultative, sharing of ideas, codevelopment level.

ZABROWSKI. We were, at times, disappointed in our relationships with CROs in the past in large part because we were using them in one-off type instances. Typically, we made decisions very late and CROs didn't have sufficient time to prepare. Many times, we gave them unrealistic timelines and, unfortunately, in the beginning they didn't push back. When there are projects that begin under those circumstances, there's going to be disappointment more times than not.

BALIAN. People in pharma haven't developed good relationships with contract research companies. Sponsors put out a request for a propos-

al for a protocol and they go through a "courting" process. What follows is a churn and burn process when expectations are not met. There are no lasting relationships.

BAID. I think there is a strong possibility of strained relationships between the contract organizations and the manufacturers in terms of expectations. Maintaining strong relationships with sponsors is becoming difficult because the pharma and biotech companies are under fire to perform and get products out on time and maintain investor expectations. This translates into higher standards and expectations from contract organizations. But we're looking at a growth trend in pretty much all of the regions, which indicates there is more work and more companies outsourcing their work.

BARNETT. The CROs don't have the trust of the industry to manage quality very well. CROs are only as good as their last project or as bad as their most recent problem. This information is what clients remember.

BOROW. As CROs have gotten bigger and bigger, they have tried to provide more services beyond their traditional areas of expertise. Consequently, priorities have frequently shifted from the "business of quality" to the "business of business" and clinical research has become a commodity rather than the expert process that it should be. In many cases, this has resulted in a divergence of goals between the CRO and its sponsoring biopharmaceutical company.

BARNETT. CROs are caught between a rock and hard place because they're being asked to provide a fairly sophisticated service, but the industry wants to treat them as a commodity. That becomes very difficult for the CROs because it doesn't matter how carefully they structure the program at the front end, there are always going to be many changes, including protocol amendments or investigators not performing quite as expected. The pharma companies would rather have the CROs take the trials off their hands. Yet, sponsors often are unwilling to listen to the CRO because they feel that they know best. In this case, the industry wants to have perfect service but at bargain prices.

Building the Partnerships

MAKRIS. How to develop a meaningful partnership is more than a million-dollar question. A partnership boils down to the attitude and mindset of both the sponsor and CRO team. The question is, does the sponsor view the relationship as a partnership or as a hiring of a labor force to execute its demands? On the other hand, does the CRO team just provide labor or does it provide expertise? Sponsors look for two things from CROs: confidence and reliability. Sponsors want to have confidence that their CRO representatives are watching for all the issues that come up during the development program and will alert them to the issues and present a resolution. This type of interaction inspires confidence; otherwise a situation arises in which the sponsor overmanages the CRO. Reliability is the second key component. Sponsors need to know that what they see today and what they will see tomorrow, in terms of quality, is consistent. Sponsors don't want to be in a continuous mode of having to track every possible detail or every possible deliverable with the same scrutiny. They need to develop a comfort level that the quality will exist from day to day. From the CRO perspective, the common issue that has been raised is that there is little recognition for their expertise. CROs are too often used just for their labor.

BALIAN. We feel it is mutually beneficial to develop better partnerships and relationships where we all can learn from our mistakes and then next

THE CONTRACT RESEARCH MARKET

YEAR	OUTSOURCE SPENDING (IN BILLIONS)	OUTSOURCED TO CROS (IN BILLIONS)	OUTSOURCED TO OTHERS (IN BILLIONS)
1999	$8.9	$5.5	$3.4
2003	13.6	9.6	4.0
2008	27.9	22.3	5.6

Source: Kalorama Information, New York. For more information, visit kaloramainformation.com.

time, we both do a better job. So instead of dumping those partnerships we're not happy with, we improve the process and the deliverables. I don't want to define preferred providers. We're not looking to give 100% of projects to one vendor. I'm looking for preferred relationships with vendors.

ANDREWS. Many outsourced projects are doomed to fail before work begins. Frequently, this can be attributed to each party making assumptions about the desired deliverable. It's important to have face-to-face meetings with the key team members to generate questions and answers about the deliverables. Vague expectations are difficult to achieve and usually create out-of-scope change orders. At MedImmune, we spend a lot of time on the relationship, defining what the expectations are and setting up metrics around that. We also train our internal folks on how to better manage the relationship.

DONNELLY. Two-way communication is important. We understand that we're only as good as some of our last deliverables. We've got to be on our toes and be forward thinking. But that said, both organizations need to be candid with each other. In any service business, that's key. For all organizations, there are going to be issues down the road. We need to be aware of those issues, and people need to communicate the good and the bad as soon as possible so that both parties can put the best people in the room and figure out the best solution. As in any partnership, once communication breaks down, there are problems.

ZABROWSKI. For the partnership to work, there needs to be an agreed upon set of expectations of what each party is going to deliver. There also has to be the necessary governance of the project and the performance against those expectations. Performance is critical for both parties to be successful. It's clear, though, that in this business there will be times, for good reason, that companies won't get the performance that they expected. At that point, it's important for the pharmaceutical company and the CRO to do an objective analysis as to why expectations weren't met, capture the learnings, and feed the information back to both organizations so that the same mistakes aren't made again.

VON RICKENBACH. The best results from a provider come over time. The better we know a pharmaceutical company's systems, processes, workflows, and culture, the more seamlessly we can provide service to them. This takes time. If companies change outsourcing providers every project, the providers may be unable to get up to speed on the learning curve.

ANDREWS. Pharma companies have to determine what type of relationship they are looking for. Pharmaceutical companies have to overcome the "them and us" mentality, and

CROs can do clinical research faster because that is what they do best. Data reveal that it is about 30% less expensive to outsource a project to a CRO than for a sponsor to do the project in-house.

AJIT BAID

CRO planning needs to be moved to the level of resource allocation, where sponsors and CROs work as a team to plan on an annual basis. This level of commitment from both sides allows sponsors to have true partnerships with service providers.

DR. BRUCE MALOFF

they have to be able to bring the external team into their internal team. The two teams have to be able to operate seamlessly. This can be done; I've seen it. Sponsors have to treat their vendors like their own employees. Sometimes, I think, subconsciously, some teams will sabotage the process because they didn't want to outsource a project. I like to measure the performance of the project team on the success of the outsourced project. This model gives our employees motivation to work with the outsourcing vendors. We set up clear expectations going into the project of what the deliverables are; we have a communications plan; and we agree to resolve issues within 48 hours so that our CRO is not waiting for us.

LANFEAR. Sponsors are looking for quality. Sponsors also look at whether the CRO is experienced and has alliances with other companies in a required service area. Pharma companies also are looking for a partner that is technically advanced because pharma companies are not data-management companies nor software companies, so they want a partner that will bring value in these areas.

HUDAK. Pharma companies should hire the best organizations they can and that's not necessarily the largest company. Big pharma companies have formed outsourcing departments that have a checklist of requirements that CROs have to meet, and smaller CROs from whom these projects get more attention don't always qualify.

LANFEAR. Pharmaceutical companies have to want to let go of some of the control. The sponsors have to understand that their expertise is in the scientific development of drugs and not in other ancillary areas. Once they understand that, the difficulty is finding a partner they can trust. It takes time to build relationships. Drug development costs millions and millions of dollars and if those relationships fail, it costs even more to start a new one.

ZABROWSKI. Both the sponsor company and the CRO must have patience in the early stages of the partnership. It takes time to nurture a relationship and to form a partnership that will survive when things don't go well.

BOROW. Pharmaceutical and biotechnology companies have to be realistic. They need to be willing to commit sufficient internal resources to allow effective and fluid communication pathways to be set up and used. After all, the drug or biologic being developed belongs to the sponsor not to the CRO. There is a very real philosophical distinction between a project that is outsourced and a project that brings in a "partner" to help expedite and improve the likelihood of success. The successful partnership starts with the development plan and the protocol not simply by handing a "fully developed" protocol to a large CRO. Moving forward, the goals need to be established to allow for trust between the CRO and the sponsor while providing a set of high-quality deliverables. The ideal partnering environment is one that encourages a collegial and interactive relationship based on common goals, an environment that is built upon professionals working respectfully with professionals.

> Some of the more successful CROs are now branching out into partnering for drug development. It is an interesting business model. It also may put a limit on growth of the service business if CROs compete directly with pharma companies.
>
> ***DR. JULES MITCHEL***

ANDREWS. If CROs think that the pharmaceutical company is being unrealistic, they need to be able to push back. We encourage our CROs to tell us if they believe our timelines are unrealistic. There are some CROs that underbid intentionally, and there is a change order before the ink is dry on the contract. The majority of the CROs that don't do that have to stand together and push back. If they deliver, then cost becomes less of an issue. We've all been low-balled by CROs that bid just to get the business.

BOROW. Pharmaceutical and biotechnology companies have to be smarter as well as more efficient as they make outsourcing choices. Some companies are establishing preferred provider relationships. Even though this makes the review process easier and more rapid for the contracts group, it may not be the best way to choose a CRO. Depending on the circumstances, the CROs on the preferred provider list may not be the best fit for a particular development or postmarketing study or program. I think sponsors need to be open to the fact that there are significant variations in size and shape between studies and that different CROs provide different capabilities and different value depending on what the program entails.

LANFEAR. If all variables are fixed, there is no way to gain efficiencies. Projects have to be flexible, at least in some variables. We have to look at delivering the highest quality first and then the most cost-effectiveness and then put the project on a timeline that is reasonable. If there is trust and when expectations are set, CROs are appreciated for the expertise they provide. We all want to get drugs to market faster, but there are myriad factors that impact the project. One example is patient enrollment. It may take 12 months to enroll 300 subjects into a study. A CRO needs to communicate challenges early on, especially if the study is more complex and it will need to send a monitor out at an increased interval and the sites are going to need additional training to get the project done right. This is the type of fixed project-management capability that CROs have to address early on.

LESTER. I don't think pharmaceutical companies truly look at outsourcing providers as partners. I think there is some minor movement in this direction, but we have a long way to go. There is a lot of turmoil in the drug-development industry right now and a lot of pressure to change the way a compound is developed because the costs are so daunting. The pharmaceutical and biotech industries need to be a little more open minded and think outside the box when bringing in service providers that have extensive experience in the real world in designing and conducting clinical trials in human subjects. So many trials fail today because of poor design and a lack of understanding of the human subject population.

LANFEAR. It will take innovative pharmaceutical people to want to change the current CRO-sponsor relationship because for too long pharmaceutical companies have treated

There is a lot of turmoil in the drug-development industry and a lot of pressure to change the way a compound is developed. Something has to change because costs are so daunting.

MICHAEL LESTER

CROs as only vendors. The CRO industry needs to communicate that it can do a more efficient, more effective job for pharma. They need to show they know the processes better and they know the therapeutic areas and can deliver the needed services more quickly. The CROs that get that message out and deliver on it will be the CROs that are the most successful in the next 15 years.

LESTER. Pharmaceutical companies can get the most of outsourcing by allowing us to become a true partner. At the site level, we are in the trenches day to day and can help our sponsors avoid some of the huge pitfalls in the conduct of their studies. We often make study design suggestions that fall on deaf ears and then six months later when the study fails, the sponsor comes back asking to be rescued. We clearly do not have all the answers. In my opinion, working together as real partners is the only way to streamline the drug-development process and ultimately lower the cost of drug development.

MORALES. Pharma companies have to start planning better. I believe that is one area where they seem to fall behind. CROs do not have the ability then to gear up or gear down as necessary to support the partnership. Planning has to begin earlier, with the CRO, medical affairs, and clinical all at the same table.

The three drivers are quality, cost, and time. Everyone wants all three. When it comes to a trial, my comment is to pick two.

DR. COLIN MILLER

HIGGINBOTHAM. CROs have made significant strides in the last few years and are better able to work with the biopharmaceutical industry because of the development of our service capabilities, global infrastructure, access to patients, and therapeutic expertise. Additionally, the pharmaceutical industry is looking to focus on core competencies and is using broader outsourcing strategies to drive efficiencies.

LANFEAR. What CROs need to do is show sponsors that they understand the need for a true partnership, that it is not just about winning one contract. Many CROs focus on getting a contract because it helps their bottom lines. They want to get that $3 million or $4 million contract today, but they're not really thinking about the $20 million that they can generate over the next five years. CROs have to build trust with their pharma company partners and be willing to take some risk.

HIGGINBOTHAM. We need to establish strong working relationships with our customers. We're looking to share their clinical-development goals. And the earlier we get involved in that process, the more value we can add. We need to have very clear outsourcing objectives, strong communications, and reasonable timelines. Measurement also is an important part of the relationship. By measuring the results of our projects, we are better prepared to meet our customers' needs.

ZABROWSKI. CROs, if they are serious about wanting to enter into meaningful relationships, are going to have to take some risks. Pharmaceutical drug-development companies and CROs are trying to achieve the same thing, which is to bring products to the marketplace faster and at lower costs. When working in this partnership, CROs have to recognize that they are an extension of the pharma company and they have to care as much about succeeding as Roche does, for example.

LANGIN. The days of being a generalist CRO have fallen by the wayside. CROs need to have project managers who are therapeutically focused. They also need to have monitors who have expertise in the specific area of focus. It's critical that CROs have the resources available to align with sponsors' needs. Many of the biotechnology, smaller and midsize pharma, and device companies want to pull in what I would define as best of breed. They want to find the best project manager to manage the project. They want to find the best CRAs. If they elect to take the electronic data capture path, they want to go with the best provider. We take on the role of setting up strategic alliances with leading vendors in those areas, be it IVRS, central labs, or EDC companies. We have established relationships with those organizations. We can still manage the project and give the sponsors complete control, while providing them the flexibility of having all the best in breed partners collaborating together.

CRO Growth Trends

BAID. The United States is the largest market for outsourcing and probably the fastest growing. The U.S. outsourcing market was just more than $4 billion in 2002. In terms of the number of CROs in the United States, there are more than 500 companies, whereas in the European market, which includes Eastern and Western Europe, there are slightly less than 400 companies with revenue of $2.6 billion. If we look at the Asian CRO market, there are an estimated 75 firms and the major concentration is in Japan. This is a nascent business in Asia right now, but it is growing, and a lot of companies are trying to build capabilities because of low costs.

MAKRIS. Much of the recent growth being experienced by CROs is related to new services, such as those that relate to preclinical, toxicology, and lab. The service centers that were initially in the big pharmaceutical companies are now becoming an outsourcing activity, a commodity within the CROs. This trend started with monitoring then moved to data, then to regulatory, then to medical expertise. Now, it's moving to the labs and preclinical services. There is a shift in the services. What pharma companies previously did in-house is now being outsourced.

BOROW. In order to be successful, biopharmaceutical companies need to increase their efficiency while containing costs. Many companies are finding that outsourcing allows them to put significantly less resources into

> What academic centers do best is help design the protocol, and the CROs are better at implementing the protocol. This would be a good partnership.
>
> *MICHAEL MORALES*

building and maintaining their infrastructure, a decision that carries less fixed costs while potentially improving process and quality.

MACMILLAN. Part of what's driving outsourcing is that CROs have a longer and better track record. Once upon a time, we might have been an unknown quantity. Pharmaceutical companies are viewing CROs as a reliable way to get some of their work done. They've worked with us, they know what our capabilities are, and they are increasingly comfortable in outsourcing their projects.

MORALES. The latest data I've seen is that 5,000 or 6,000 patients are required per NDA, up from 1,500 patients in the early

1990s. Pharma companies are not equipped to handle the recruitment of such a large number of patients or larger numbers of investigators.

HIGGINBOTHAM. There is a correlation between pharma industry R&D spending and the performance of the CRO sector. As we have seen in other industries such as IT and finance, a changing business environment also

We're seeing a much stronger drive toward quality and efficiency. We're becoming a more mature, established industry. Our customers are expecting a certain deliverable.

PATRICK DONNELLY

Outsourcing is not going to solve the problem of productivity because productivity is something the pharma companies have to solve on their own.

DR. SAMUEL BARNETT

There is a lot of value in developing long-term partnerships with one or two of the multinational CROs. This helps us understand each other's processes and culture, and we believe this also will improve efficiencies and bring our products to the market faster.

DR. DAN ZABROWSKI

encourages a move toward strategic outsourcing. My view is that market conditions are getting much tougher. The industry is facing more modest growth, more pressure to perform, and increased regulatory hurdles. As a result, our customers are focused on core competencies and trying to reduce development risk. They are looking to CROs for new skills and new technologies to help them address these challenges.

BARODY. CROs, particularly small or medium-sized companies, can execute research much more efficiently because of their size. They are not encumbered by the bureaucracy of a large company. Decisions can be made more quickly. The other thing to keep in mind is that CROs have a profit incentive, unlike a research division, whose only job is to spend money. CROs need to be extremely efficient in what they do.

MAKRIS. Being a representative of a niche service provider, I would claim that a sponsor doesn't need a full-service CRO to handle all its needs. There are many other CROs that are niche providers, which is evidence that the system supports the need for niche providers.

MORALES. The FDA has formulated guidelines that require pharmaceutical companies to develop a risk-management plan. As part of those plans, there is a requirement to conduct usual-care evaluations because the agency wants to see how a drug is going to perform in the real world. Sometimes, well-controlled trials are almost too well controlled. There are narrowly defined inclusion/exclusion criteria and companies don't bring in a broad enough group of patients. Companies generally are geared toward conducting traditional Phase II, Phase III, and some Phase IV trials. They generally aren't equipped to handle studies with 25,000 patients and 3,500 investigators.

MILLER. Another reason for growth in the outsourcing sector is that pharma is contracting specialty services. Historically this wasn't done. There has been an increase in the number of requirements from the FDA, such as ECG and imaging, which has resulted in more outside contracting.

BARODY. Pharmaceutical companies use CROs to fill gaps, but the gaps typically are in terms of manpower, not necessarily therapeutic expertise. They may come to us because they don't have a monitoring organization and they need an army of monitors, but they would not necessarily come to us because they have a gap in oncology expertise. I think that clients could make better use of what we have to offer by picking our brains on therapeutic expertise. For example, we have more than 50 oncology nurses in our organization. We know a thing or two about how to conduct an oncology study and that knowledge is available for the asking.

TAAFFE. CROs can respond faster because there are no distractions. Many pharmaceutical companies have a matrix management model. The development teams are involved with the marketing people, who are involved with early phase planning. This creates internal competition for resources. When companies outsource, the team has no distractions and is driven by deadlines.

BOROW. We are beginning to see a shift within the biopharmaceutical industry from companies maintaining tight internal control over the critical design process to a more intellectually open and best-in-class approach to

trial design. After all, the success of a clinical trial or development program is often determined to a large extent before the first patient is even recruited. For example, the proper selection of the primary efficacy variable, determination of sample size, and selection of subject inclusion or exclusion criteria are all absolutely critical to a study's ultimate success.

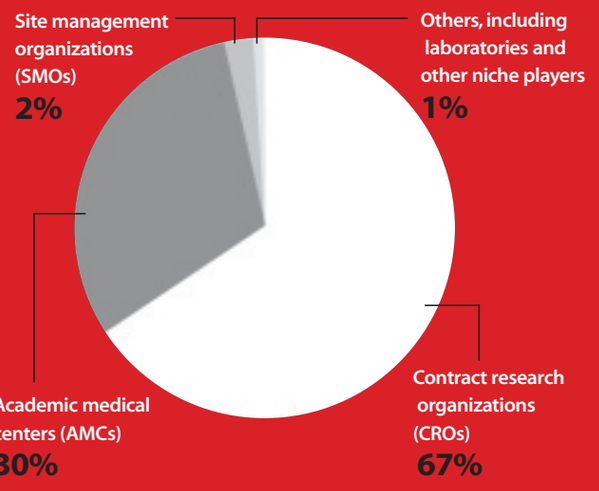
TAAFFE. Pharmaceutical companies are outsourcing full development programs. And if a CRO doesn't have broad capabilities, it will not be in the mix. From the pharmaceutical company's point of view, this is a more efficient way to outsource. By partnering with a CRO that has a variety of services, the company gains efficiencies, as well as a bundling discount for the various services, including lab, clinical, IRVS, and data management.

HUDAK. Large pharmaceutical companies have fewer compounds in the pipeline, so they are doing more Phase IIIB and IV work. And they're farming out much of that work.

MAKRIS. The reasons why small pharmaceuticals and big pharmaceutical companies outsource are slightly different. Big pharmaceutical companies have much more challenging pipelines now. By that I mean, in essence, they have to replace very big products with huge sales with products that don't have big sales. In this situation, these companies have to maintain their fixed cost structures. Thus, they can't build immense service centers, and they need to outsource to keep costs down. For the smaller biotech companies, it's very hard to convince an investor that significant resources should be put against in-house service centers, when they know there are many outsourcing options. These are some of the reasons why the CRO sector is expected to experience significant growth.

MALOFF. As consolidation in the CRO and pharma industries continues, CROs with broader capabilities have emerged. But even global CROs have to focus on core capabilities in running trials and managing data. As the demand for acceleration in clinical trials continues to drive new types of research services, such as electronic data capture and hand-held patient diaries, pharma is looking for CROs to play well with others. CROs and specialized service companies that provide integrated solutions make it easier for pharma to gain efficiencies. As these alliances continue to evolve, there is a win-win situation for pharma and CROs.

CONTRACT RESEARCH MARKET SHARE BY ORGANIZATION TYPE IN 2002



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CRO Challenges

MACMILLAN. CROs have to deliver really solid service and quality. We have to keep in mind that a service company has to deliver good service.

BOROW. Many of the challenges CROs face today are very similar to those encountered by the pharmaceutical and biotechnology companies themselves. We are all evaluating new technology solutions to optimize processes in order to assist in the delivery of quality products on time and within budget. Ultimately, we must define how to best move from innovation to clinical practice. This will require a marriage of basic science, pioneering technology, operational expertise, and government guidance in an effort to make product development and, ultimately, commercialization possible.

MAKRIS. The challenges in the future for CROs will mirror what's happening in other sectors, including the outsourcing of labor to other countries. This means that CROs have to use technology more effectively to eliminate duplicative tasks or eliminate labor for tasks that can be more efficiently handled by technology.

DONNELLY. What keeps me awake at night is the rogue CRO, a company that might be a little loose with FDA regulations, and loose with how it performs a trial or site visit. The FDA will audit that trial and find all types of problems and then there is a knee-jerk reaction against CROs. Then pharma wants to bring projects back in-house. I worry about that because this is something I can't control. I can control our teams, I can control hiring, and I can be involved in the competitive atmosphere. I have no problem going up against our ethical peers, but the companies that veer off the accepted path because of financial or other reasons concern me. When any service provider gets a black eye, people start looking at the whole industry.

MALOFF. CROs are in a highly commoditized space. The industry is mature. CROs are regulatory driven, and sponsors have a challenging time differentiating them. A walk around the exhibit floor at the annual meeting of the DIA finds each CRO proclaiming experience, performance, and customer focus. But the ultimate expense in a clinical trial is time; some CROs are attacking that problem early on in the process. Trial acceleration should start at the preclinical level, with CROs facilitating gene expression analysis to select compounds with minimal risk and to avoid tanking because of toxicity or metabolic issues. Similarly, CROs can facilitate patient enrollment and study start up by incorporating better patient phenotype and genotype criteria, then working with sponsors to design protocols that take into account pharmacogenomic variations. I think this is the secret to a CRO being able to evolve as a fully integrated research and development partner, bringing resources to bear that change the way trials are done.

LESTER. Research sites need to be paid fairly and timely. One of the biggest challenges, especially for sites, is the fits and starts of the industry. Cancellations and delays are a huge problem, particularly when we've committed resources to a study and, more importantly, when we have study subjects who have committed to participating in a study. Research sites across the United States are closing their doors every day because of cash-flow problems. Sites cannot continue to be used as a source of funding for the pharmaceutical industry.

MAKRIS. The biggest challenge is resource allocation. CROs are challenged by the possibility of

CROs are in the relationship business. We deliver service and that service is delivered by people. If our people aren't trained and if we don't give them the tools and technologies that allow them to succeed, our sponsors are not going to be pleased with the quality of work.

BRIAN LANGIN

We spend a lot of time on the CRO relationship and defining the expectations, as well as trying to set up some metrics around those expectations. We also train our internal people on better management of the relationship.

CONNIE ANDREWS

the sponsor pulling the clinical trial. Then the CRO has a group of people who don't have a job anymore. The risk has been shifted from the sponsor to the CRO. This becomes a resource management issue. Retention of resources is another challenge. With a hundred companies providing outsourcing services, there is a lot of competition for quality people. This environment relates back to the relationship between the sponsor and the CRO. People need to feel that they have ownership in the process and their work; this helps keep them motivated. But if people feel they are just day-to-day labor without any association to the ultimate goal, then CROs compete strictly on salary.

TAAFFE. The ebb and flow of the pipeline is another challenge. Most CROs usually rely on four or five clients, and the ebb and flow of their pipelines has to be considered. To cope, CROs have to have a wide range of services. CROs need to be able to cross train their people and move people from medical research to data management or from project management to IVRS or to the lab.

MALOFF. Information technology management is a real source of delay in clinical studies. If we look at pharma companies' preclinical divisions, they've embraced ultra high-throughput screening procedures. They are doing data analysis on a million data points a day in a very technology-driven manner. If we move over to the clinical side of the organization, most are still recording data by hand using three-part forms. Data analysis and data queries happen weeks later, with subsequent slow resolution as the data are reviewed one site at a time. This results in enormous inefficiencies, not just in terms of capturing the data, but in terms of the hours, weeks, and months of time wasted chasing paper and not using progressive approaches to clinical IT. CROs are moving this process ahead with e-clinical solutions, focusing their monitoring teams on improving site performance and data-management teams for dose-ranging studies and go/no-go decisions.

BAID. One of the challenges that CROs face is recruiting and sustaining good-quality employees. From our analysis, people recruited on a contract basis might lose their jobs if there is less work. CRO recruiting techniques are going to be very important. And, simultaneously, the CROs need to have a very elaborate sales and marketing network and business development teams that can ensure that they sustain continued business to retain quality employees.

BALIAN. CRO turnover is an issue for all of pharma. We believe the approach we are taking, where the CRO employees, in essence, will take ownership and accountability for the work, will help CRO employees feel more valued and perhaps reduce the turnover rate. CROs need to commit to hiring a good staff and retain them for a particular pharma sponsor.

LANFEAR. Staffing turnover becomes an issue when CROs lose their senior people. These are the people they need to focus on keeping. The project manager, the senior data manager, and the clinical study managers are the people a pharma company builds a rapport with. When these people change, when these team members are lost, it affects the relationship with the CRO and therefore the drug-development program overall.

ZABROWSKI. We are very mindful of the turnover within the CRO industry. We also assess financial stability and determine whether there is a strong management team. If the CRO has reasonable stability on the financial front and a strong management team, then the likelihood is that there will be less turnover. That obviously creates less disruption and improves the continuity for projects, both in terms of our relationship with the CRO and, more importantly, their interaction with our investigators. Investigators like continuity. They want to see the same people coming to talk to them about the clinical trial and not a "monitor of the month."

MACMILLAN. In the late 1990s when the economy was really strong, we had more turnover than we would have liked. We've looked at that pretty hard because retention of good staff is good for everybody. It's good for the employees to have a place where they like to come to work, a place where they feel engaged and needed and well paid. In absolutely every survey and every discussion we have with clients they say they want consistent project teams. For the last two to three years, we've paid a huge amount of attention to retention.

In the future, the challenges that CROs will face mirror what's currently happening in other service sectors, including outsourcing of labor to other countries. This means that CROs have to focus on building and maintaining their competitive advantage and compete on strength of expertise rather than labor force.

DR. LUKAS MAKRIS

DONNELLY. CROs have a different orientation and they attract a different type of person, usually someone who is more entrepreneurial. I tell every senior person I interview — and many of these people are coming out of pharma — that there will be constant change. Most likely, the job a person will have next hasn't yet been thought of. If this is an environment that people feel comfortable with and will thrive in, then this is the place for them. But if someone needs a five-year career path, that's difficult.

BAID. One of the strategies that CROs are adopting to retain good employees is enhancing the education offerings to their staff. They're increasing the knowledge base. They also offer flex time and telecommuting.

LANGIN. Sometimes sponsors will hire good people right out of a CRO. So CROs have to be very careful how they present their team to sponsors. In retaining high-caliber individuals, CROs need to be sensitive and realize that people have families and lives outside of their careers.

BAROODY. In the past, CROs had an image of being second class compared with drug companies and sometimes had reputations of being sweathouses. Because of the mergers of pharmaceutical companies, more people have recognized that the concept of job security at a pharmaceutical company is a myth. I think top-notch people in the clinical-research industry are becoming much more open to working at a CRO.

MITCHEL. CROs need to be flexible. They have to be able to move in and out of different businesses and move their people around. They need to cross train people. The idea is not to lay people off. There are certain areas where CROs won't be able to cross train. They can't make someone a physician or a biostatistician. If people are willing to be somewhat flexible and not be pigeon holed into particular jobs, this can work. For example, a CRA could help in medical writing. But, this takes a lot of organization and flexibility on the part of the CRO.

MAKRIS. It's very difficult within the pockets of expertise that are needed for the different areas to cross train personnel. We can't train a data monitoring person to be a statistician or vice versa. There might be some areas where CROs can move people from one position to another, but there are some areas where this is not at all possible. ✦

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