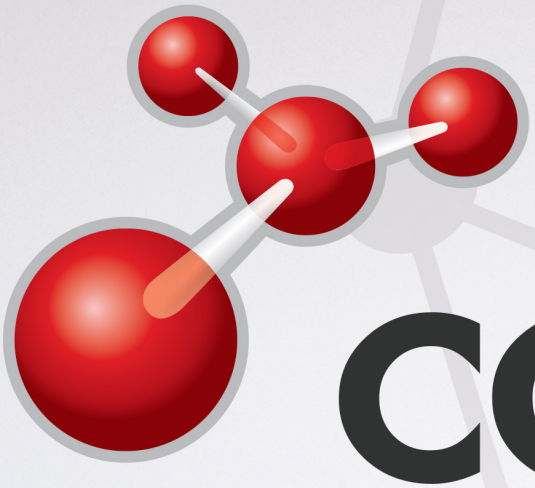

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DEVELOPMENT AT OUR CORE

CONTRACT DEVELOPMENT: 3 CASE STUDIES ON ACCESSING EXTERNAL INNOVATION

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Contract Development: 3 Case Studies on Accessing External Innovation

Outsourcing has become a huge business, with Frost & Sullivan estimating the pharma industry spent $13.4 billion on contract manufacturing and development services in 2013. Many outsiders assume price is the primary motivation of all this outsourcing, but in an industry in which the bestselling drugs bring in more than $1 billion a quarter, it makes little sense to risk delays by making decisions based solely on cost. The reality is the best service providers offer more than just financial flexibility.

All service providers free pharma companies from the need to invest in in-house infrastructure and staff , outlays that could prove to be a complete waste if the project fails. However, surveys, such as a poll of 61 biopharma R&D decision makers by analysts at Jefferies & Co, typically find price is just one of three important factors. In the Jefferies poll, results from which were published in May, price was the second most important factor in outsourcing decisions, behind expertise and just ahead of breadth. Companies want good value, as opposed to cheap, service providers that can benefit their business through more than just cost savings.

Industry interest in the breadth and depth of service provider expertise has increased in recent years as even the biggest pharma companies have recognized the need to look outside their walls for innovation. The dream of building fully integrated pharmaceutical companies has faded, with all of the big firms now working with a network of third parties to discover and develop drugs. An acceptance that the scientific skillset needed for 21st century drug development is beyond any single company is a motivating factor for the shift. Having made the move to a more networked model of innovation, companies must learn how to get the most out of their service providers. In this paper we analyze three recent client relationships at CoreRx and their lessons for the broader outsourcing sector. Each shows how firms can tap external expertise to benefit drug development, the best practices that enable these relationships, and the pitfalls that can undermine the process.

Case Study 1: How to Effectively Outsource Innovation

Contract development organizations (CDO) work at the coal face of pharma R&D and as such often learn about new products and technologies first. Open minded pharma companies can tap into this knowledge. CoreRx recently encountered such a situation in which a client asked about development Contract Development: 3 Case Studies On Accessing External Innovation Janice Cacace, Ph.D. Director, Formulation Development. CoreRx, Inc. of an extended-release product for a Phase I trial. Turnaround time was vital. Having recently learned of a new co-processed excipient that enables directly compressible formulations with different release profiles, CoreRx proposed using the product on the Phase I project. The client had the flexibility to use any compendial grade excipient and as such went ahead with the novel approach.

Using the excipient, CoreRx quickly produced tablets with three different release profiles, allowing the client to start the Phase I study within six months. The approach also offers potential intellectual property benefits to the client. However, while with hindsight the project was a clear success for the client, CoreRx, and the excipient supplier, many factors can stop such innovative win-win programs from coming to fruition. Picking a CDO that was attuned to new technologies and free from the formulary limitations some companies place on excipient selection got the client off to a good start, but even at that stage the project could have unraveled.

The program worked because both parties clearly communicated their needs and capabilities. In some cases a client will sign off on a quote with excipient compatibility included, only to later reveal their team already knew which components they wanted to use. The client in this case study was clear about which excipients were acceptable and open to innovation within those constraints. Having a clearly defined project from day one is the basis for success. A service provider needs to know what the client wants, and the client needs to know the capabilities of the service provider. If a service provider can only process 8kg per batch but you need 2 tons a year, look for a more suitable partner.

Case Study 2: When a Service Provider Should Say "No"

A top-tier service provider will try to shape its capabilities to the client's needs as much as possible, but should be willing to speak up when a project is too far outside its area of expertise. CoreRx recently had a situation like this, in which a client needed a solvent-based process in order to maintain its API in the amorphous state. Specifically, the client wanted the process to be wet granulated in a high shear mixer, and dried in a fluid bed. This would involve transferring the wet solvent-containing mass in a concentrated state into the fluid bed and then initiating drying. CoreRx can handle such a process on a small scale for development, but it would be impossible to transfer to the manufacturing unit.

CoreRx proposed two alternatives, the first of which utilized a unique process involving a high shear granulator and nonaqueous solvent system. The second proposal involved spraying onto a substrate using a fluid bed process. Both would have allowed CoreRx to take on manufacturing. They Contract Development: 3 Case Studies On Accessing External Innovation offered other benefits, too, notably the ability to control the evaporation rate and limit the solvent concentrated in any one process. This cut the risk of explosions compared to the client's preferred approach. After discussing the matter with CoreRx, the client chose to stick with its original process, a decision that meant it would need to find a new service provider for production.

While CoreRx will never back down from a challenge — a fact demonstrated by the proposal of two alternatives to the client — there comes a time when it is better to walk away, even if it means losing business. The scale-up process is hard at the best of times, with nobody truly able to predict what will happen. For example, when moving from a 100g development batch of petrolatum based suspension to a 100kg commercial batch, it is very difficult to predict how long it will take to achieve uniformity. With such inherent uncertainties common in scale-up, it is unwise for a service provider to take on work for which it is ill-equipped. Even though the client is always right, sometimes "no" is the best answer.

Case Study 3: Why it is Best to Fix Problems Early

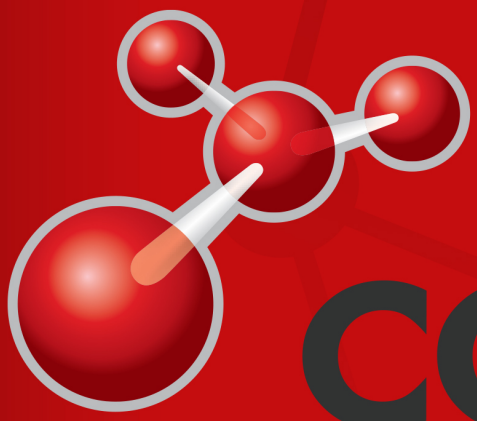
Working with a diligent, questioning service provider from early in development can save a company headaches later. With pharma companies under pressure to speed drugs into and through clinical development, staff can overlook problems. Listening to the opinion of an objective, less emotionally involved service provider can help a firm recognize which of its early stage problems will lead to bigger, more time-consuming and expensive issues down the line if left unresolved. CoreRx has seen the consequences of ignoring problems. Having raced to the cusp of Phase III, a client is now facing up to the fact that production of its drug is constrained by a long dwell time for tablet compression.

The press on which the product is manufactured could operate at three times the speed the client is achieving, but the rate is being limited by the compression process. If the compression problem was fixed early in development, it would have caused a short, low-profile, and relatively inexpensive delay. Now, with the product about to enter pivotal late phase trials, the client is left wondering whether it is possible to fi x the problem without changing the formulation. If the formulation changes, regulators could class the revised version as a new product, setting back development time lines. The risks of acting are high, but the risks of continuing to ignore the issue are greater still.

Such a no-win situation could have been prevented by acting sooner. No client wants to hear bad news from a service provider, but the onus is on CDOs to provide an experienced and objective view of the risks and benefits of a particular approach. Instead of viewing problems uncovered early in Contract Development: 3 Case Studies On Accessing External Innovation development as setbacks, both parties should think of them as opportunities to put the perfect processes in place while the stakes are relatively low. Finding problems in early development suggests the process is not robust enough to cope with scale-up. By optimizing the process before scale-up, the likelihood of a smooth transfer to commercial-scale production increases.

The Importance of Flexibility

Each of the case studies shows how in client-service provider interactions — as in formulation decisions — it is impossible to take a one-size-fits-all approach. The needs of each client and characteristics of each drug are too varied for such a homogenous way of working. While formulators will often start with a mix that worked well on a previous project, the final product will be shaped by the drug's morphology, solubility, and other characteristics. Similarly, while a service provider will learn from successful client relationships, the exact details of each partnership will be dictated by the needs of the customer. The best service providers listen to the needs of the customer, clearly define the parameters of the project and their capabilities, and use their unique position in drug development to propose novel, innovative solutions. By communicating their requirements and being open to new ideas, pharma companies can tap into a wealth of drug development experience while saving money.



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