

Perfect fit

Even the largest pharmaceutical companies do not have sufficient in-house research capabilities to discover the next therapeutic breakthrough. Partnering with contract research organisations is essential, but managing these relationships has its pitfalls. Abi Millar talks to **Frances Grote**, Millennium Pharmaceuticals, about how to achieve excellence within outsourced relationships.

When business professor James Quinn dubbed outsourcing ‘one of the greatest organisational and industry structure shifts of the century’, his words were more than mere hyperbole. Indeed, as the practice grows more widespread, it is becoming virtually indispensable. A high proportion of companies now outsource at least some of their operations, and the market for contract research organisations (CROs) is estimated to be worth \$29 billion.

Nowhere is this more the case than in pharmaceuticals, in which outsourcing has changed from a niche pursuit to one of the bedrocks of the industry. With drug development beset by spiralling costs, and companies experiencing diminishing returns on their R&D investments, classic ways of doing business are starting to seem untenable.

“It now costs anywhere from \$800 million to \$1.1 billion to get a drug to market,” says Frances Grote, senior director of outsourcing at Millennium Pharmaceuticals.

“All companies are scrambling for ways to reduce that total. Part of that reduction would be lowering your fixed priced cost, which means that you outsource instead of having your own personnel.”

Riding the outsourcing wave

Millennium, a Massachusetts-based pharma and biotech company with a focus on oncology, is riding the crest of this outsourcing wave. Delegating not just some, but all of its operations to three different CROs, it is in many respects the prototype of a 21st-century pharma firm.

The company has long recognised the value of business partnerships; since its inception in 1993, its development has

been dominated by the instigation of new strategic alliances. It was a merger with Leukosite in 1999 that brought the company’s first drug, Campath, tantalisingly close to market. And when Velcade was granted approval several years later – the first treatment for multiple myeloma in more than a decade – this was on the basis of a low-priority project started by Leukosite and brought to the forefront by Millennium.

Not until 2008, however, did Millennium’s current business model fall into place. The company became a fully owned subsidiary of Japanese pharma giant Takeda, and along with the merger came a dramatic broadening in scope. With a level of growth impossible to accommodate in-house, Millennium began to outsource in earnest.

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“We don’t have a global presence ourselves, but we want to file our drugs, hopefully simultaneously, in multiple global markets,” says Grote. “For us, the principal advantage of outsourcing is to get expertise, balance and resources in markets where we don’t have our own personnel.”

This shift has had major ramifications for Millennium's in-house workforce. Rather than conducting processes themselves, their role is now one of leadership, with staff overseeing and managing established operations while themselves spearheading change.

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“I don't know if we are 100% successful in our vision as yet,” says Grote. “It's easy enough to say to our employees they have to delegate authority to the CRO, but at the end of the day, people feel a personal responsibility for the quality of what's being done. We're still working on training our team about the best ways to delegate authority.”

Benefits and challenges

The impact on a company's existing personnel is just one of the challenges posed by outsourcing. For all the probable benefits, outsourcing throws up a whole new dimension of potential complication, and success or failure largely hinges on how well companies manage relationships with their CROs.

Should relations turn sour, they're unlikely to effectively harness the new intellectual capital at their disposal.

It is the job of Frances Grote and her team to ensure that Millennium works harmoniously with its partners. This task is far more complex than overseeing a single, vertically integrated organisation. Because CROs are independently structured bodies in their own right,

the emphasis is on ensuring that nobody is working at cross purposes. Key to this mission is effective communication.

“The most basic and fundamental level of communication is project team to project team, following an integrated model,” says Grote.

“This means that we and the CROs have trained our teams to work together, as opposed to Millennium outsourcing and then using the outsourced resources.”

While a CRO should not be regarded as a replica of its sponsor, if the two teams work collaboratively then something of the company culture may be assumed to translate. This is

crucial; because the risks associated with outsourcing are often attributed to a sponsor's loss of control over the process, it is vital that that sponsor remains integrally involved.

This involvement is by necessity bureaucracy-laden. A strong company culture depends on adherence to shared values, and while such values are often unspoken, if a firm is outsourcing, it needs to make them overt. The first step, then, is to define goals and motivate the CROs to stay in line.

“We have multiple levels of goals here at Millennium,” says Grote. “We start out by sharing all of these with the partner CRO, and we make some of the payment milestones in their contract contingent upon achieving them, so they have a financial incentive to support our goals.”

Next, you need to implement strong systems of governance, making sure leaders communicate on a regular basis. Millennium holds quarterly meetings between governors from both sides of the divide, giving them a forum to air any operational and strategic issues that have arisen.

Finally, a formalised conflict resolution process should be put in place.

“We have a representative at Millennium, not concerned specifically with outsourcing, whose job it is to mediate if necessary,” explains Grote. “And if that's not sufficient then we have an issue escalation pathway that allows project teams to rapidly get guidance from the most senior levels of both organisations.”

Working as one

While communication is essential if you're looking to foster warm relations, the ultimate aim is loftier. In an ideal world, there would be full transparency between the parties, with discrete organisations working together as an integrated whole.

In Millennium's case, all its CROs are conceptually committed to this cause. In fact, two are public companies, which means that Millennium can clearly see their business models and work out how its own numbers feed into theirs. Their third CRO, however, is private, and as such is not legally required to be so forthcoming.

“We have to ask them for financial information, which they're not obligated to give,” says Grote. “Although we have a pretty good idea what their mark up is and how that translates into profit margins, we really don't have full visibility on their cost structure.”

In such instances, a number of the particulars can only be taken on trust. Lack of transparency is a perturbing issue in the precarious world of drug development. With few guarantees that an investment will yield results, a sponsor organisation needs to find ways of ensuring it's not being swindled.

As well as the risk of fraud, hazards include loss of data, delays in study completion and various types of regulatory infraction. In short, the consequences can be serious.

One way around this problem is to enter into a risk-sharing arrangement. The CRO takes on part of the financial burden of drug development, in return for ownership of the drug once it goes to market. Or, under an alternative model, the CRO is not paid upfront, but rather receives a royalty in return for the services it provides.

While such strategies are commonplace, Millennium is taking a slightly different tack.

"We have chosen instead to minimise our financial risk by controlling what we spend on our contract," says Grote. "We've instituted a model where our own estimates are binding unless we ourselves have issued a change in scope."

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This is something of a novel approach in a marketplace in which, historically, CROs have had free reign to alter their terms of contract. For the most part, these companies have tended to issue a change in scope if their initial budget turned out not to cover all their profit margins. Millennium, however, retains its own best estimates based on a long process history of performing operations in-house.

From strength to strength

Outsourcing is in many ways still subject to experimentation. It is a relatively recent shift, propelled to a large degree by the

pace of technological change. As the scientific landscape becomes more specialised, it becomes increasingly harder to develop the necessary depth and breadth of scope in-house. And as investment cycles are compressed, there is greater pressure on pharma companies to develop drugs at speed.

This trend shows few signs of abating. Frances Grote for one envisages that the growth in outsourcing will continue. She is adamant, however, that the models in place at present will be subject to change.

"CROs developed in an environment where sponsor companies wanted CROs to function as mirror images of themselves," she says. "So, if the sponsor had 'x' kind of personnel doing the job in a certain way, they would demand that their provider had the same kind of personnel before they handed it over.

"What I think the entire industry has discovered is that it's not very efficient. We don't have a real efficient model yet for how to develop drugs, but there are lot of people working on what that model might be. In the future, things will be far more consolidated, with multiple service offerings from one source. I'd say that once someone has figured it out, the outsourcing industry is going to be in a much stronger position." ■

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