COMPOUND MANAGEMENT: THE NEXT FOCUS FOR OUTSOURCING?

Outsourcing has become increasingly popular as pharmaceutical companies have sought to cut fixed costs. Compound management has, however, tended to remain in-house, despite not being a core part of drug discovery. Why, until recently, was this the case? And why are things now beginning to change? **Tim Lease** and **Mike Stock**, Biofocus DPI, explain.

Pharmaceutical outsourcing is growing at approximately 15–20% annually. Until recently, however, compound management accounted for a very small part of this growth, despite it not being a core component of drug discovery. Instead, most medium and large pharmaceutical companies still manage their compounds in-house and spend up to hundreds of millions of dollars investing in new equipment, building new facilities, buying in expertize, or keeping their current processes up to date. This is because such organizations see their compound library as their 'crown jewels;' a key piece of their intellectual property and a valuable material resource for drug discovery. When outsourcing was still relatively new, these companies weren't sure that they could trust another organization to protect such a valuable asset. For example, they were worried that a confidential compound might mistakenly be shipped to a competitor. In contrast, many small companies do not think about compound management until they have been operating for a while without an organized system in place and realize this needs to change.

A New Era — Change is in the Air!

Pharmaceutical companies — in particular, biopharma — have become more familiar with outsourcing, and are increasingly scrutinizing any proposed investment in capital and labour to see if it can be outsourced cost-effectively instead. Managing their compound collections is creeping onto their radar as they realize that compound collections can be treated in a similar manner to functions that they have already outsourced. For example, their reagents and stockrooms are routinely managed by external companies, and they routinely share intellectual properties and materials to solve medicinal chemistry problems.

One of the compound storage systems

In addition, recognizing the value of their growing collections, companies can be nervous about operating without backup copies stored at a different location. They are also beginning to appreciate the level of expertize that companies that provide outsourced services can bring to their processes.

One situation in which outsourced compound management should be considered is when a pharmaceutical company realizes it needs to update its compound management facilities and equipment; this is a big investment, so outsourcing can be a lot cheaper. Another circumstance that can prompt outsourcing is after a merger between two pharmaceutical companies, corporate restructuring, or the purchase of a new facility. Compound libraries will almost certainly need to be moved between sites — or brought together into a single library. This is often a daunting task, leading to internal management conflicts, which can be solved by taking the 'neutral' outsourcing path.

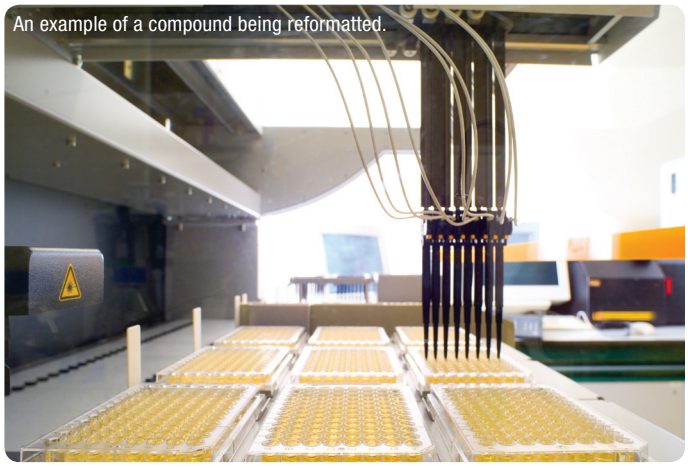
Small companies, meanwhile, will often reach a 'tipping point' where they realize they need a compound management strategy, but are nervous about buying in the people and resources required. Early on, such companies typically store their compounds in domestic freezers and remove them manually. However, as they acquire larger numbers of compounds, having staff rummage through the freezers becomes too labour intensive and can be prone to human error. Again, it's not as simple as merely moving compounds from place to place; very often the management system has been 'ad-hoc' — so many small companies are turning to external specialists for help.

Finally, start-ups, whose management has come from big pharmaceutical companies, tend to think about compound management at an early stage. The management realize they will need to adopt a compound management strategy eventually and are keen to minimize the capital investment required. If they have finite cash resources, they will invariably want to spend as many funds as they can on drug development, and as little as possible on storage infrastructure.

Taking it Outside

There are three main ways in which companies approach adopting a compound management outsourcing strategy. The first is to store compounds at an outsourced facility. This is cheaper and less trouble than alternative approaches, but has the potential disadvantage of taking a company's material and intellectual property off-site.

Furthermore, the company concerned needs to think about the location of the outsourced facility. Distance matters because samples need to be close enough to be reliably shipped 'just in time' for screening. However, with good


An example of a compound being reformatted.

Running the NIH MLSMR for the NIH

In July of 2008, BioFocus DPI's contract to run the Molecular Libraries Small Molecule Repository for the US NIH (National Institutes of Health) was extended for a further two years.

Jamie Driscoll, Chief of Research Services in the National Institute of Mental Health's Division of Neuroscience and Basic Behavioral Science and Project Officer for the contract, explains the original reason for contracting the management of this compound library: "The NIH MLSMR collects samples for high throughput biological screening and distributes them to the NIH Molecular Libraries Probe Production Center Network. This is comprized of sites spread across the US that were successful in bidding for grants to carry out screening within the Molecular Libraries Initiative. This is an NIH Roadmap project supporting 'new pathways to discovery in the 21st Century.' As results are generated, they are made available for public access."

"When we embarked on this project we soon realized we did not have the expertize or the equipment needed to manage the 300,000 compound library. As we were unsure what the lifetime of the project would be, it did not make financial sense for us to start investing in the expensive infrastructure we would need to manage and distribute the compounds efficiently from scratch. Furthermore, we were not convinced that we could install the equipment and recruit required expertize within the timelines we had set for this project," says Driscoll.

"We therefore considered outsourcing to be a potential solution and invited interested parties to respond to our requirements. We received several proposals, and these were all reviewed by an external panel of experts. At the end of this process we selected BioFocus DPI as our partner because of the high technical merit of their proposal and reasonable costs."

Driscoll continues: "Once a year, BioFocus DPI sends all the participating screening centres an entire set of the library contents. Each quarter, they receive an update comprising compounds that have been added to the collection. The standard delivery format for samples is as 'mother plates' ready for high throughput screening, but other 'cherry picked' samples are sent out for hit follow up. In total, we ask BioFocus DPI to send out approximately 5–10,000 cherry picked samples every month. The company also carries out all the necessary reformatting and performs regular QC on the samples to ensure they are still in a good condition."

"Outsourcing the management of our repository has proved to be a very effective solution; it has also allowed us to maintain a flexible approach to the storage and distribution of these important samples," adds Driscoll.

logistics, there is no reason why compounds cannot be stored in the US for European customers, and vice versa. Since a carefully selected outsourcing partner can ship compounds out as quickly and reliably as bringing the compound from an internal store, there is no reason not to outsource.

The second is to "in-source" or employ an independent organization to run a compound library in-house. This keeps intellectual property in-house, removes the headache of compound management and brings in valuable external expertize. It is, however, likely to be more expensive than taking everything off-site.

Finally, outsourcing specialists can be employed as consultants to help a company meet the challenge of managing its compounds in-house. However, good outsourcing specialists can provide more than just storage. They can also assess the quality of a compound collection during outsourcing and at agreed intervals afterwards. Stored compounds can often be in poor shape because they have decomposed over time or have not been stored correctly. Alternatively, they might have been bought a long time ago and were not of good enough quality to begin with.

In general, experienced outsourcing partners have the specialist skills available to handle samples correctly; but outsourced compound storage specialists can help ensure the process is more efficient and less damaging. For example, one problem that needs to be managed is the damage usually associated with repeatedly freezing and thawing compounds in preparation for screening. As part of the outsourcing contract, the compounds can be expertly reformatted into individual microtubes or other containers. This means that only the sample required for the desired screen needs to be accessed, preventing damage to the rest of the compounds in the library. Alternatively, samples can be repackaged and reformatted onto various formats of microwell plates so that they can go straight into screening without the pharmaceutical company concerned needing to do any further processing.

Compound Management in Action

BioFocus DPI — the service division of drug discovery company Galapagos — has secured a growing number of compound management contracts from organizations with large libraries. For example, it operates the US NIH's (National Institutes of Health) MLSMR (Molecular Libraries Small Molecule Repository, see boxed story, left) and the US EPA's (Environmental Protection Agency) ToxCast (Prioritization of Environmentally Relevant Chemicals) programme library. The former is a US Government funded project to develop molecular probes as tools for drug discovery by collecting samples and making them available to a select network of research organizations, for high-throughput biological screening. The project has recently been extended with the launch of the NCC (NIH Clinical Collection) — a collection of 446 known drug or drug-like bioactive compounds that have a history of use in man and are thought to have undiscovered bioactive and therapeutic potential.

The Way Forward

Compound management is not a core function of drug discovery and, recognizing this, pharmaceutical and biotechnology companies are increasingly considering outsourcing when starting or restructuring a storage facility. As the market grows, the opportunity for outsourcing companies to deliver new and innovative services is growing too. For example, in the future, outsourcing firms may go into partnership with logistics companies to bring off-site compounds on-site faster and more efficiently than ever before. For companies that have not yet taken this step, there has never been a better time to consider outsourcing compound management. **Pharma**

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