

# IN OR OUT?

**PDA's Anita Derks and Georg Roessling tell Lorrie Kelly about the pros and cons of contract manufacturing and in-house production when it comes to keeping costs down and getting products onto the market.**

**A**s pharmaceutical companies seek quick and cost-effective ways to bring new products to market, contract manufacturing organisations (CMOs) are experiencing a boom in business. However, this may prove to be short lived. Anita Derks and Georg Roessling of the Parenteral Drug Association (PDA) believe pharmaceutical giants are likely to bring specialised technologies back in-house over the longer term in a bid to control costs, quality and IP issues.

‘CMOs are busy when there is marketing or manufacturing at a commercial scale,’ says Anita Derks, global quality manager (biotechnology), PDA Biopharmaceuticals Conference Speaker. ‘A lot of companies aren’t capable or don’t have the capacity for making products themselves, so they outsource. However, I don’t think this is a permanent situation, but more likely a quick option.’

‘There is a skill set involved in CMO facilities that gives pharmaceutical companies a greater opportunity. It doesn’t make production cheaper; it’s a capacity issue. With a blockbuster product, for example, you would have better cost if you manufacture in-house, but the flipside to that is you have to pick your location very carefully because there are often huge tax implications. Because of this, I think there will always be a significant demand for CMOs, particularly in development products and clinical material manufacture.’

## Big vs small

The economic decline, combined with ever-rising costs related to clinical trials and regulatory systems, has placed more pressure on big pharmaceutical companies to streamline their business processes. However, Derks believes the emphasis on cost effectiveness may not be as high on the agenda as it could be. ‘In big pharmaceutical companies, the business model doesn’t often change,’ she says.

‘For instance, how can a CMO or a generic company compete with big pharma? The reason is they have lean processes; they have a very low scrap rate and high success rate. They don’t invest a lot of time or money in profit improvement because they are just doing what the customers ask. Plus they are able to keep their facilities full. Most CMOs are multi-production facilities, but big pharma can also contract dedicated facilities, especially for drug substances.’

In the long term, Derks sees the current trend towards outsourced manufacturing as an opportunity for pharmaceutical companies and CMOs alike, with the end result being more standardised processes. ‘I think standardisation helps in reducing costs and increasing flexibility,’ she says. ‘Since the cost of setting up a facility and building a facility are the same, that can’t be a factor. It must be how the facility is used that creates the difference in costs. I think that outsourcing manufacturing is a very positive thing because it is pushing companies to truly understand their production and manufacturing processes, and it allows pharmaceutical companies to focus on the things that are important from the technical and patient safety perspective.’

Georg Roessling, senior vice-president of PDA-Europe, believes that although the trend towards CMOs will continue, more and more companies are finding strong arguments for resuming in-house production. According to Roessling,

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## Contributor profile



Since 2002 Anita Derks has worked in human pharmaceutical quality roles in various countries, focusing on bioscience businesses and special projects such as establishing quality approaches for vaccines and advanced therapy medicines. She is now global quality manager for biotechnology at PDA.



Georg Roessling has been the senior vice-president of PDA-Europe since 2006. Prior to this, he worked for 21 years in the pharmaceutical industry with 15 years as head of parenteral development at Schering AG, Germany. He is also a member of GDCh, Bunsengesellschaft.

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the future of CMOs will depend very much on the strength of their business models and how easily they can adapt to new and emerging technology gaps within the market. ‘CMOs who produce specialised products will become stronger and have the best growth potential,’ he says. ‘Within pharmaceutical companies there will remain quite a bit of production. It will never be a situation where everything will move towards outsourcing. There are a few pharmaceutical companies, at least from the management side, where the goal seems to be sourcing cheaper places to manufacture. However, some are starting to reconsider this focus because there have been problems, including critical issues with intellectual property rights.’

### Merging and minimising

In the US, pharmaceutical companies are continuing to reduce manufacturing capabilities and relocate those capabilities to Europe or Asia. Roessling thinks that the more important trend is that companies continue to merge or are bought. In these scenarios, they often have a big number of manufacturing sites which are costly. ‘For example, I have seen companies with 100 manufacturing arms and their goal is to reduce this number to 30,’ he says. According to Roessling, the ultimate goal is not only to reduce the number of manufacturing centres but to also restrict manufacturing to specific sites. Rather than having ten facilities around the world manufacturing one product, there would be one specific site that would produce a single product for the global market. ‘This strong focus on fewer manufacturing sites will compete with the CMOs,’ he continues. ‘Consolidation will compete with outsourcing, and the CMO capacity will never reach a level where they would be able to take over pharmaceutical production entirely. CMOs are more useful for smaller-scale manufacturing.’

On the regulatory side, particularly in the ICH regions Europe, Japan and the US, there will be changes because of new regulations that allow for a continuous improvement of the production over the lifetime of a product. This will change the way development and production people have to work together. This environment can prove challenging for the traditional CMO/pharmaceutical company relationships where development functions and manufacturing have worked in mutually exclusive spheres with minimal communication. In the past, the goal was to develop a process, transfer it to the manufacturing department, validate it and not change it any more. A change in the production resulted in a complicated, time-consuming and costly process to get approval from the health authorities for such a change. Pharmaceutical companies had an established process, which

### CENEXI'S VIEWS ON CONTRACT MANUFACTURING ORGANISATIONS

Though many believe pharmaceutical companies will eventually bring production back in-house, Nicolas Micheaud of Cenexi, a CMO under the parent company of Roche, predicts that CMOs will continue their rapid growth by filling production gaps.

‘There are fewer blockbusters entering the market now, and not as much in the pipeline in terms of big products that can sustain companies on their own,’ explains Micheaud. ‘All of big pharma are looking at their mature products as potential revenue spinners. I do not think there is any economic gain for outsourcing products at the beginning or middle of their lifecycle, but after this, why not?’

Micheaud believes the way to improve on manufacturing cost is either through synergy (keeping production in-house) or by rationalising the manufacturing through dedicated facilities that supply a single product for the entire market. It will probably still be necessary to go to someone who can do more, such as a CMO.

‘There are different needs for pharmaceutical companies: the need to handle the old, mature products and the need for development,’ he says. ‘For CMOs to succeed, they must constantly question their capability.’

was passed on to the manufacturing site without further communication between the development and manufacturing teams.

‘The manufacturing people were told to stick to the process without changing anything,’ says Roessling. ‘Now there is a continuous push to improve processes within the pharmaceutical industry. Through this, over the lifetime of the product, companies can decrease the production cost significantly.’

### Focus on production

According to Roessling, the long-term effect of this will be that pharmaceutical companies will potentially be able to produce end-of-life products at a much cheaper cost than CMOs, making it far more difficult for generic companies to remain economically viable. ‘If you look at the political landscape, everyone talks about how there should be biogenerics and biosimilars,’ says Roessling. ‘This will happen in the near future within the US. So there is definitely a strong

drive to reduce cost, including production costs. In the past, companies would say that they don’t deal with production; it is a very small contribution to the overall costs. Now, pharma companies are thinking of production costs and I’ve seen examples where they could cut the costs by 70% or more. To be able to do this you need close co-operation between development, quality and manufacturing; if you were to outsource it would be quite difficult for a CMO to make the continuous improvements required.’

Roessling believes that high-value products will not likely be outsourced in the future. There could be a period when pharmaceutical companies outsource because they lack the capacity in-house. But overall, companies will stick closer to production because they can see opportunities to increase the lifetime of their older products and avoid competition from generics. ‘This is all extremely complicated,’ he explains. ‘There are so many trends that are superimposed that to give a simplified answer as to whether in ten years we will have 50% of production done by a few CMOs who continuously produce day-in and day-out, would be difficult. But I think it is very unlikely. Pharmaceutical companies understand how important it is to have in-house expertise from production and development. Also, because of Quality by Design, companies will be reluctant to share strategic knowledge quickly or easily with others.’

‘I imagine that in five to ten years, pharma companies will recognise that it is more cost effective to keep production in-house,’ Roessling concludes. It is certainly more than just direct production cost aspects that influences the decision whether or not to work with a CMO. **WPF**