

INSIGHTS

Manufacturing the Future

Integrated Collaboration between Contract Manufacturers & Pharmaceuticals

The life sciences industry has traditionally relied on the foundation of a few key blockbuster drugs and premium prices to drive profits while they actively pursued the next game-changing drug approval. For years, pharmaceutical companies have prospered on generous margins and new breakthroughs during thriving economic periods, but times have changed. Continuing patent expirations and diminishing pipelines have altered the way pharmaceutical companies have to do business in order for them to invest in research and development. Strategies that reduce costs and are easily adaptable have become increasingly important. This paper addresses one such cost optimization strategy—contract manufacturing.

Contract manufacturing is a strategy that many pharmaceutical companies are presently using to meet the new challenges. In the *2009 Annual Outsourcing Survey by Contract Pharma*, 29% of respondents said that more than 50% of their commercial (final dosage) manufacturing is currently done by contract manufacturing organizations (CMOs).¹ CMOs have become a necessary part of the life sciences value chain because their design reduces costs by:

- Offering flexibility
- Providing expertise
- Reducing the internal requirements needed to support manufacturing

Even though CMOs are being used today, they are being managed in a similar way as they were during the 80's and 90's. This management and market reality creates complexities in the strategy that have thus far prevented it from reaching its maximum potential. Using CMOs allows a pharmaceutical company to shed internal practices, but it now has to adopt the management of external relationships – sometimes including 10 or more participant sites for complex processes such as biological product manufacturing.² As leading pharmaceutical companies expand their value chain to include CMOs, they're faced with numerous communication challenges (see Figure 1, next page).



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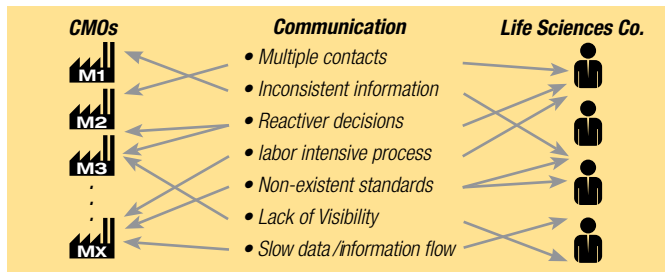


Figure 1: Current Pharma-CMO Communication

Many of the difficulties are a result of CMOs becoming rapidly adopted as cost-effective solutions for pharmaceutical manufacturing with little attention to developing optimal relationships. Additionally, utilizing CMOs inserts another step in the process and puts the security of the pharmaceutical companies supply chain—the single most important element—at greater risk.

Pharmaceutical companies seeking to drive profitability and flexibility from CMOs require innovative ways to manage their operations. They must re-invent the processes and technologies used to support the CMO model in order to create integrated collaboration between the two partners and mitigate the current deficiencies. Integrated collaboration will allow market leaders access to timely and accurate information for improving manufacturing and provide a foundation for enhancing supply chain security. CMOs that work to build integrated collaboration with their pharmaceutical company partners differentiate themselves and increase market share in a fragmented market, while pharmaceutical companies that are willing to engage in integrated collaboration can reap financial benefits.

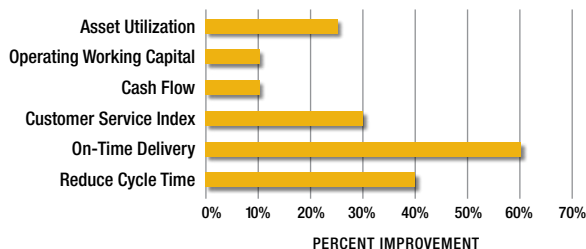


Figure 2: Improved Financial Measurements

Source: Clarus Information

Mounting pressure on life sciences

Current trends and potential new requirements are contributing to the consistently demanding life sciences industry. Some of the issues that presently impact the industry include:

- Shrinking pipelines
- Expiring patents
- Counterfeit drugs
- Increased regulatory scrutiny on profits

Additionally, the government has revealed some of its intentions for the pharmaceutical industry through legislation discussions on price caps and universal health care that will impact market strategies. As if the new challenges weren't enough, any change that a pharmaceutical company wants to make is going to be subject to the ever-present requirements of safety, efficacy, quality, and cost. Leading executives must understand how the direction of the life sciences industry will impact the future value chain of pharmaceuticals so they can start positioning their organization for greater profit.

The future value chain of pharmaceuticals

The current and future trends of the life sciences industry are going to re-allocate work to different value chain areas based on need. Some essential parts of the current value chain are unlikely to change, including:

- Regulatory
- Quality Assurance
- Finance
- Human Resources

Other parts of the value chain are more likely to use other options, such as contractors and external partners to accomplish necessary tasks because they are more flexible and specialized to the market needs of the time. Certain parts of the value chain may also see increased or decreased investment based on the trends of the time. Based on the current pharmaceutical value chain and the mounting pressures on the industry, the future of drug development is likely to involve three changes:

1. Manufacturing excellence
2. Increased manufacturing
3. Production responsiveness

Manufacturing excellence

In the pursuit of higher margins, pharmaceutical companies will set goals to increase security of supply and reduce production costs. A research report by Marsh found that 91% of outsourcing-intensive pharmaceutical participants had a “significant incident” (i.e., causing a loss of \$10,000 or more) due to quality problems or delays with contract partners, compared to only 59% of peers whose operations are mostly in-house.³ Companies must find better ways to produce and protect their products—manufacturing excellence is part of the solution.

Manufacturing excellence is essential because it ensures a production process is:

- Stable
- Consistent
- Predictable
- Flexible
- Safe
- Efficient
- Cost-effective

These characteristics help a pharmaceutical company meet their goals by:

- Decreasing deviations
- Reducing the time required for normal manufacturing activities
- Shortening corrective action time
- Increasing on-time delivery

Establishing manufacturing excellence will also help life sciences companies be prepared for new government influences and regulations. The government will advocate products that are produced via a secure and cost-conscious supply chain. In the event that universal health care, price caps, or other initiatives are implemented, these products and their organizations are well-positioned.

Increased manufacturing

A rising population and evolving market will necessitate an increase in pharmaceutical manufacturing to meet the demand. The world population has increased from 3 billion in 1959 to 6 billion in 1999, and is expected to continue to grow. Current projections show the population expanding by approximately one billion people or 17% over the next 10 years.⁴

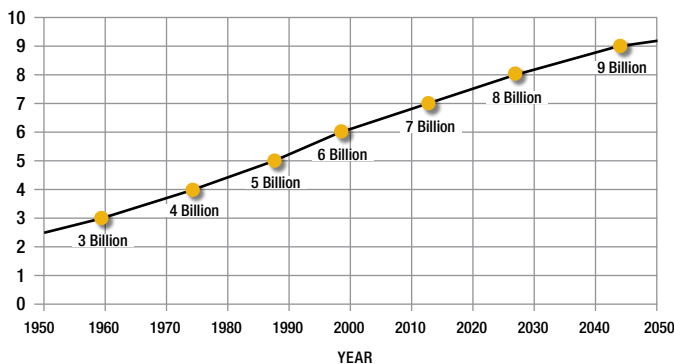


Figure 3: **World Population**⁵

Three factors are contributing to the population growth and escalating demand:

1. Aging baby boomers – the elderly require the highest medical attention.
2. Longer life spans – greater time periods for treatment.
3. Greater exposure to health care – emerging countries are making advances in health care that are enabling greater access while a shift to universal health care in the United States could further expand coverage.

Production responsiveness

An impending change to the future of drug development is the ability of pharmaceutical companies to quickly adapt their manufacturing capabilities (size, locations, and products) to market, industry, and organizational changes – production responsiveness. New regulations, emerging market opportunities, and new technologies are all factors calling for production responsiveness, but a primary driver is capacity utilization. Higher capacity utilization requires more agile and flexible operations.

Typically, pipeline efforts focus on the most promising drug, not on finding the drug which fits a capacity need. Adjusting manufacturing capabilities to focus on a set of complementing



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manufacturing technologies instead of comprehensive services can provide matching demand from multiple feeders. The benefits include:

- Increased utilization
- Higher proficiency
- Greater predictability
- Lower costs

Production responsiveness will also help pharmaceutical companies in other important ways:

- Shorten the time required for small-scale production of drugs to support early clinical trials
- Create the right drugs at the right time (most recently highlighted by the H1N1 outbreak)
- Support a diverse and balanced product portfolio

Why CMOs are attractive

Given the likely future changes to drug development, CMOs are uniquely positioned as a differentiating solution. Consider the benefits and challenges of using CMOs in the following table.

Benefits	Challenges
<i>Qualified/expert personal</i>	<i>Supply chain security</i>
<i>Optimized product-specific processes</i>	<i>Scheduling</i>
<i>Current equipment and technology</i>	<i>Multiple contacts</i>
<i>Reduced facility, energy, maintenance, changeover, and headcount costs</i>	<i>On-going data exchange (inconsistent information, non-existent standards, slow, labor intensive, reactive, lack of visibility)</i>
<i>Globalization</i>	<i>Initial tech transfer</i>
<i>Regulation specialization</i>	<i>Exposed intellectual property</i>
<i>Increased capacity</i>	
<i>Higher capacity utilization</i>	

The benefits of CMOs are aligned with manufacturing excellence, increased manufacturing, and production responsiveness, which is why they are currently entrenched in the life sciences value chain and poised for growth.

Jim Miller, president of PharmSource and monthly column author for *Pharmaceutical Technology* magazine, said that the manufacturing excellence business model is the most critical differentiator for the CMO industry. CMOs can help pharmaceutical companies achieve manufacturing excellence by providing specialized expertise in the production processes to reduce costs while still maintaining quality and security.⁶

The fact that the CMO design can address a plethora of future changes makes it, at the very least, an option to strongly consider despite its shortcomings. As the life sciences value chain changes, CMOs are in a position to be the standard solution, especially as their relationship with pharmaceutical companies evolves to mitigate the current challenges.

Evolution of the CMO-pharmaceutical relationship

The CMO-pharmaceutical relationship began as a tactical solution when large pharmaceutical companies used CMO sites for capacity overflow or cost dilution. Due primarily to quality issues with the initial arrangement, a central governance of all CMOs was created as the next tactical step of the relationship to provide quality assurance. Recently, the supply chain has taken the lead on the CMO-pharmaceutical relationship to build a global network – another tactical transition. The present phase in the evolution of the CMO-pharmaceutical relationship is the strategic simplification of the network by focusing on fewer suppliers. As the world continues to evolve, so must the model in which pharmaceutical companies utilize internal manufacturing and a disorganized group of CMOs. Pharmaceutical companies need to reinvent the CMO relationship in order to prepare for the future, and the following is how they can begin:

1. Evaluate CMOs to determine the best in class.
2. Establish a network of CMO partners.
3. Reinvent the relationship.
4. Develop an enabling technology for actionable information flow.

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Evaluate CMOs to determine the best in class

No CMO has consumed a majority of the market, which means that pharmaceutical companies looking to use a CMO need to establish a prioritized list of the requirements they expect a CMO to meet. Most of the evaluation can be based on standard manufacturing criteria, but don't forget to consider culture, as it plays a big part in building a tight relationship. Another important question to ask is whether or not the CMO is open to sharing detailed information if a trusted solution can be established. This is important for building future collaboration. There is ample documentation available on the topic of selecting a CMO, as it varies greatly based on the company and the type of manufacturing, so this paper will defer further discussion on the matter to other resources that provide a more detailed analysis.

Outsourcing advisory – business case

When it comes to outsourcing manufacturing, many consumer products companies have already undertaken the decisions, management, and technologies associated with CMOs. One CP company, a leading, global player in mobile communications hardware and software, looking to better compete in the industry and adapt their business strategy to take advantage of contract manufacturing, came to Clarkston for assistance. Clarkston helped:

- Develop the methodology for an outsource manufacturer selection
- Establish KPIs between the company and outsource manufacturer
- Identify KPIs measurement processes and associated reporting output tools
- Select the optimal provider based on the company's business objectives
- Create the work-plan, roles/responsibilities, business case, and governance structure
- Manage the transition of processes to the outsource manufacturer

The results of establishing a successful outsourcing relationship included:

- Lower operating costs estimated at \$1,000,000 per year
- Performance improvement measured by performance scorecard
- Improved brand loyalty
- Better focus on core competencies
- Improved consumer satisfaction

Establish a network of CMO partners

The future of the CMO-pharmaceutical relationship is going to be a network of partnerships between a pharmaceutical company and CMOs. The pharmaceutical company is ultimately accountable for effectively managing every CMO in their network, so they must build trusted relationships with a select number of preferred CMO vendors who give them the greatest value of service while closely protecting their intellectual property. Preferred vendors are a vital piece in the network, since they provide unique advantages to the pharmaceutical company and CMOs greatly desire the security of the distinguished title.

Preferred vendors offer leading drug companies an avenue to increase data transparency and share more ideas as a result of their level of business comfort. CMOs seek to be preferred vendors because it positions them for a growing revenue stream. The 2009 Annual Outsourcing Survey conducted by Contract Pharma reported that 55% of respondents said that they use only 1-5 preferred vendors for outsourcing and 49% said that over half of their outsourcing dollars go to preferred vendors.⁷

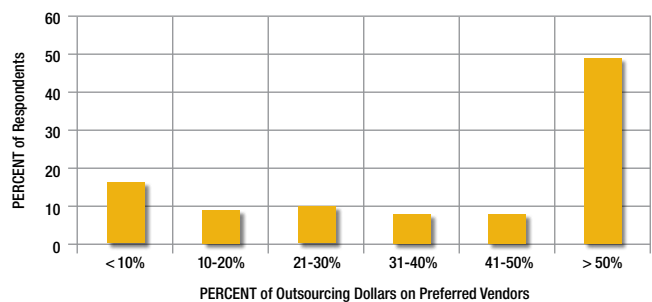


Figure 5: Outsourcing Dollars

Reinvent the relationship

It has always been in the pharmaceutical company's best interests to work with their CMO network to optimize their operations and ensure that they are providing the maximum return on investment, but the complexity of the future network demands a new level of involvement. Some of the factors that will require a pharmaceutical company to better manage their CMO network include:

- Larger number of specialized CMOs to evaluate
- Global CMO locations
- Increasing regulatory considerations
- Sharper attention to cost reduction

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For a pharmaceutical company to achieve the greatest benefits, it must reinvent the relationship through persistent discussions with their preferred partners on planning, common objectives, and the responsibility of operating more effectively against key metrics.

Pharmaceutical companies must work with preferred CMOs to agree upon performance measurement criteria with key performance indicators (KPIs) or other metrics to help both organizations track their success while providing goals and direction for future growth. Developing criteria together will give both partners an opportunity to better understand the other's culture, glean new insights on operational efficiencies and manufacturing practices, and most importantly, build trust. In establishing a trusting relationship, pharmaceutical companies can expand their collaboration to planning and the sharing of real-time transactional data such as:

- Advanced shipment notifications (ASNs)
- Quality notifications
- PO confirmations

Once a pharmaceutical company can view its CMOs as an extension of its organization, it can include them in strategic decision-making processes and facilitate data transparency as partners.

Manufacturing Scorecard Items

- | | |
|--------------------------------|-----------------------------|
| • Inventory Levels | • Scrap and Rework |
| • Perfect Product Quality | • On-Time Delivery |
| • On-Time in Full | • Average Cycle Time |
| • Production Downtime | • Fixed Manufacturing Costs |
| • Variable Manufacturing Costs | |

Develop an enabling technology for actionable information flow

Technology is now capable of integrating one or more different systems together and providing decision-making information via a single portal. Visionary leaders will leverage this enabling technology to facilitate the management of multiple CMOs through a singular system.

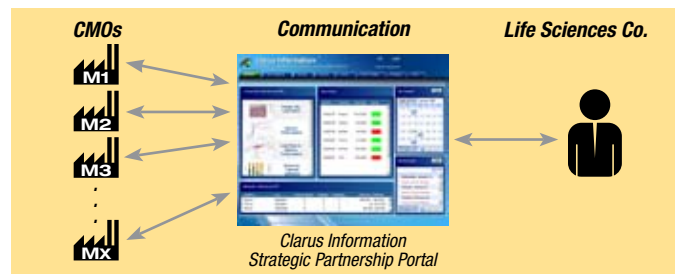


Figure 6: **Single BI Communication Point**

Business Intelligence (BI) software is the primary tool for combining information from various data repositories and displaying it in a number of powerful dashboard views for an end user to review. In order to best manage their network of preferred CMOs, pharmaceutical companies should implement a BI software system and take advantage of the opportunity to incorporate their preferred CMO partners in jointly establishing a portal that will allow them to share defined information in real-time.

A BI solution will reduce the complex management issues of using CMOs and provide integrated collaboration between the pharmaceutical company and multiple CMOs. Utilizing the compilation of information displayed in a BI solution, the pharmaceutical company and CMO can:

- Execute against clear expectations – Both companies will be required to determine exactly what information is needed by the other. Once configured, a BI solution will allow both companies to actively work towards defined goals and each will be accountable for meeting pre-established metrics.
- Reduce risk – quality and supply chain security risks of inconsistent data due to a lack of standards are resolved through a BI solution that requires strict conformance. A rigid software configuration will result in one version of the truth.
- Increase predictability of product supply – a BI solution will resolve any issues in data format inconsistencies and allow a user to view all associated data for product supply in a single window to facilitate a well-informed prediction.
- Provide timely information sharing with faster response times – information can be automatically gathered from various sources and displayed in multiple views. The portal provides all organizations an immediate single-access point to the critical data defined throughout the configuration.



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- Share the responsibility of operational excellence – a BI solution creates a transparent platform for inventory, expiration, and manufacturing data that holds all organizations accountable for making improvements as a result of the visibility.

A major benefit of developing a BI solution is the platform it provides for increasing supply chain security. The visibility and open design give the pharmaceutical company the ability to check, track, and trace product and supplier information on a regular basis. This will allow them to avoid security issues or catch them earlier in the process and reduce their impact. The timely and accurate information provided by a BI solution also will allow for continuous risk evaluation and continuous improvement. In addition, as the life sciences industry develops more structured supplier certification standards, pharmaceutical companies will already have the technology in place to access the information.

Integrated collaboration through a BI solution also will help pharmaceutical companies quickly provide technology transfer to preferred CMOs through reliable information and established communication. Daniel Smith, who touts the criticality of collaborative communication for technology transfer between a pharmaceutical company and the CMO client in his article “Handling a Risky Business: How to Ensure Successful Technology Transfer”, says:

“[I]t’s not just clear communication that is essential—it is just as important that an atmosphere of open, two-way sharing is fostered between the sending and receiving unit. It is not unusual for sending parties to be nervous about sharing all the data related to their product, especially if there is negative data, but once confidentiality agreements are in place, there should be no need for hesitation. Holding back information can invite unforeseen challenges further down the line.”⁸

Considering the fact that CMOs differentiate themselves on three main things—service delivery, manufacturing excellence, and ease of business—a solution for integrated collaboration is a particularly striking prospect for CMOs because it helps in all three areas. CMOs will be able to strengthen their service

value by sharing information in a more effective manner and mitigating the complexity challenges they pose to pharmaceutical companies. Having a BI solution in place will provide clear metrics and goals for the CMO to aspire to, thereby driving manufacturing excellence, and ensuring their continued success.

An innovative partner for CMO-pharmaceutical collaboration

Clarus Information is a solution that combines manufacturing and quality information that improves the transparency of your organization and allows best-in-class communication between service providers and their partners.

Clarus Information has been developed by a manufacturer of pharmaceutical and biotechnology products. Companies can leverage the knowledge and experience that was used to design a leading edge communication platform capable of quickly connecting your manufacturing and quality information from various systems and securely providing web-access to key information to internal stakeholder and external partners.



For more information on Clarus, visit www.clarusinformation.com or contact Mike Brookman at mbrookman@clarus-information.com.

For more information, visit: www.clarkstonconsulting.com or contact Rob Klein 877-362-3649 / rklein@clarkstonconsulting.com

“Pharmaceutical manufacturing will be performed in the future in a (neuronal) network of high performing suppliers. The question of whether or not the supplier is a part of a particular pharmaceutical company will be secondary. The ability to adapt to ever changing requests while maintaining high quality/compliance standards and delivery performance will be the differentiator.”

Hans Engels
President & CEO
DSM Pharmaceuticals

Conclusion

Pharmaceutical companies who seek to be at the forefront of drug development must pioneer a new way of managing their operations to boost profits. CMOs are a vital part of the future life sciences value chain and pharmaceutical companies must reinvent their processes and technologies to take full advantage of their services. Industry leaders will assemble a network of CMO partners that are aligned with their organization, and identify preferred partners who are trusted to most effectively execute on the firm's goals via integrated collaboration.

A BI solution for integrated collaboration is a revolutionary new concept that provides transparency to the pharmaceutical supply chain, which can be a true win-win for both the CMO and pharmaceutical companies. Creating a network of CMOs

that can operate with a pharmaceutical company through a single platform will permit pharmaceutical companies to meet the changing demands of the future.

The life science companies that seize the opportunity to share information, develop standards, and implement a BI solution will set a precedent and reap the benefits. Only two questions remain:

1. Which pharmaceutical company will be first to evolve and thrive through integrated collaboration with CMOs?
2. What CMOs are ready to commit to integrated collaboration and emerge as market leaders?

Both questions will soon be answered as pharmaceutical companies reinvent their manufacturing strategies and discover the vastly undeveloped potential of integrated collaboration with CMOs.

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