The State of the Biopharma Contract Manufacturing Industry

Assessing the Impact of COVID-19, Industry 4.0 and Flexible Design

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Growing and Innovating: The State of U.S. Biopharma Contract Manufacturing

The demand for biopharma contract manufacturing services is at an all-time high. So how did we get here, and where is the industry going?

The increased reliance on biopharma contract manufacturing organizations (CMOs) has been driven by various cost-saving and efficiency-building incentives for biotechnology and pharmaceutical companies, including:

1. Lower production costs
2. Reduced manufacturing footprint
3. Dynamic manufacturing capabilities
4. Increased speed to market
5. Reduced risk
6. Fewer capital expenditures
7. Access to specialty equipment and processes

All these factors, plus the increased demand for biologics, are contributing to a projected near doubling of the North American biopharmaceutical contract manufacturing market over the next several years, from a valuation of $6.2 billion in 2019 to an anticipated $11.75 billion by 2027.[1]

Biopharma Contract Manufacturing Market Snapshot

North American market size 2019:	**$6.2B[1]**
Expected North American market size 2027:	**$11.75B[1]**
Global market size 2019:	**$13.73B[1]**
Expected global market size 2027:	**$25.5B[2]**
Number of global CMOs:	**235 and counting[3]**

While contract manufacturing has been on the rise for many years, the COVID-19 pandemic caused an undeniable shift in demand for CMOs, with both positive and negative implications.

Continue reading for more on the impact of COVID-19, industry projections, trends to watch over the next decade, and tips for selecting a CMO.

Capacity and Capabilities: Four Factors Influencing the CMO Market

Not long ago, CMOs operated as manufacturing extensions for larger pharmaceutical companies that needed to increase production capacity.

With growing demands, rising costs, and increasingly complex technologies, CMOs are in a more strategic position to serve as skilled providers of the industry's most advanced manufacturing processes, giving biopharma companies access to expertise and equipment often not feasible to procure internally.

Throw in a pandemic that disrupted the global supply chain, and you have a recipe for the reinvention of an entire industry.

Here is a closer look at four factors influencing the CMO market dynamics.

1. Increasing Demand for Biologics

The biologics segment accounts for the largest share of the North American biopharmaceutical CMO market, with the continued success of biologics and FDA approvals breeding even greater research and development efforts.[1]

Due to the increasing complexity of upstream and downstream processes and the technologies required to produce these sensitive products, CMOs are uniquely positioned to win an ever-growing percentage of biologics manufacturing work.

Top 50 Global Pharmaceutical CMOs[4]

1. AbbVie Inc Company
2. Aenova Group Company
3. Ajinomoto Bio-Pharma Services Company
4. Alcami Corporation Company
5. Alkermes Biotechnology company
6. Almac Group Company
7. Aurobindo Pharma Ltd.
8. Avid Bioservices Inc.
9. Baxter Biopharma Solutions Company
10. Bayer AG Company
11. Biocon Limited Company
12. Biomay AG Company
13. Biophore India Pharmaceuticals Private Limited Company
14. Bora Pharmaceuticals Company
15. C.H. Boehringer Sohn AG & Ko. KG Company
16. Cambrex Corporation Company
17. Cardinal Health, Inc. Company
18. Catalent Pharma Solutions Inc.
19. Cepia Sanofi Company (Parental of Sanofi)
20. Charles River Laboratories International, Inc. Company
21. Consort Medical plc
22. Corden Pharma International Company
23. Daito Pharmaceutical Co., Ltd. Company
24. Delpharm SAS Company
25. Divi's Laboratories Ltd
26. DPT Laboratories, Ltd. (Mylan N.V.) Company
27. Dr. Reddy's Laboratories Company
28. Evonik Degussa Company
29. F. Hoffmann-La Roche Ltd
30. amar S.A. Company
31. Fareva Pharmaceuticals Company
32. Fujifilm Diosynth Biotechnologies (Merck & co subsidiaries)
33. GlaxoSmithKline Pharmaceutical Company
34. Huapont Life Sciences Co Ltd Company
35. Koninklijke DSM N.V. (Royal DSM) Company
36. Lonza AG Company
37. Nipro Corporation
38. Pfizer Company
39. Recipharm AB Company
40. SAFC Biosciences (Merck KGaA Subsidiaries) Company
41. Samsung Biologics Company
42. Siegfried Holding Company
43. Strides Pharma Science Limited Company
44. Teva Pharmaceuticals Company
45. Therapure Biopharma, Inc. Company
46. Thermo Fisher Scientific Inc.
47. UPM Pharmaceuticals Company
48. Vetter Pharma Company
49. WuXi AppTec Company
50. Zhejiang Hisun Pharmaceutical Company

The expense of building and operating flexible, state-of-the-art facilities is cost-prohibitive for most biotech and pharmaceutical organizations, both virtual companies with no in-house manufacturing and larger companies without specialized facilities. Outsourcing to a CMO makes sense in both scenarios as companies look to limit their risk until their products are proven enough to justify in-house production.

Not only does outsourcing manufacturing operations make financial sense from a capital perspective, but it also allows companies to focus their resources on their value-added core competencies — like research and development, marketing, and strategy — with the goal of speeding time to market and expanding access to novel therapies.

One area where CMOs are particularly poised for growth is in cell and gene therapy production, where technology and regulations are quickly becoming complex and burdensome. Manufacturing expertise of cell and gene therapies is limited, and CMOs represent the best and sometimes only option to get a new therapy to market. With 1,220 regenerative medicine and advanced cell and gene therapies in clinical trials worldwide as of February 2021, this is a major opportunity for CMOs.[5]

Monoclonal antibodies are soon expected to account for half of the molecules entering the clinical pipeline, with viral vectors and other cell and gene therapy molecules making up an additional 23 percent.[6] Beyond cell and gene therapies, CMOs can also capitalize on other emerging technologies in need of manufacturing expertise, such as biofabrication and regenerative medicine.

2. Advances in Technology and Manufacturing Processes

The rapidly rising demand for active pharmaceutical ingredients (APIs) requires a level of innovation and flexibility not built into existing manufacturing facilities.

Gone are the days of constructing large-scale, all-steel facilities that mass-produce the same drugs over and over. Here to stay is the flexible facility that allows for easy scale up/scale down and quick turnover from one process to the next as technology adapts and production needs change.

Within the outsourced model, companies also avoid the need to commission and qualify new equipment and keep facilities up to date as the technologies advance. Companies can also shop around and choose multiple specialty CMOs that best fit their needs.

To meet the demand that biopharma companies have for the production of cell and gene therapies, CMOs are changing the way manufacturing is done. A flexible facility incorporates some or all of the following components to meet the varied needs of today's pharmaceutical and biotechnology leaders:

- Moveable equipment
- Single-use technology
- Automation
- Artificial intelligence
- Modular design
- Prefabricated pods
- Knockout wall panels
- Exposed utilities
- Independent HVAC systems

Specialization and flexibility allow for faster and more efficient production by CMOs, helping pharmaceutical and biotechnology companies focus on R&D while ensuring production moves rapidly.

"Since contract-based projects are milestone-based and depend on the successful delivery of results, an unsuccessful project can be terminated early, while successful projects can be transferred to clinical and commercial manufacturing significantly faster than at a traditional pharmaceutical company.

So, the main advantages of contract manufacturing and outsourcing are rapid development of innovative drugs and faster launch of clinical and commercial manufacturing."[7]

Vadim Klyushnichenko, Ph.D.
Former VP of preclinical services and process development
Paragon Bioservices

3. COVID-19 Pandemic Shockwaves

When the COVID-19 pandemic began, there was a near-immediate impact on the biopharma supply chain as access to critical components was limited or non-existent.

Biopharma companies had to balance the instantaneous global call for COVID-19 vaccines and treatments with the challenge of meeting demand for the medications people rely on daily to survive — all while struggling to procure the needed materials.

On the upside for CMOs, there was an unprecedented amount of outsourcing for vaccines, led by headline agreements between AstraZeneca and Emergent BioSolutions and Johnson & Johnson and Catalent. For biopharma companies like Pfizer that chose to manufacture COVID-19 vaccines themselves, CMOs still benefited from the outsourcing of traditionally in-house manufactured products to free up space.

The pandemic also brought many drug supply shortages, mostly resulting from anticipatory purchasing, temporary factory closures, and the reliance on overseas suppliers for 80 percent of raw materials used.[8] In 2020, there were 833 drug shortages reported by the FDA — although not all can be attributed to COVID-19-related supply chain disruptions — compared to 377 reported in 2019.[9] Fifty-seven percent of the 2020 shortages were reported in April and May.[9]

COVID-19 also reopened the conversation on reshoring pharmaceutical manufacturing with renewed vigor and urgency. As politics are so heavily intertwined in the topic and ultimate decision on reshoring, don't expect action anytime soon. However, the lines of communication remain open and the call for regional and sustainable supply chains is clearer than ever.

Many believe the COVID-19 vaccine push was just the tip of the iceberg when it comes to CMOs' potential growth over the next several years. However, the increasing reliance on CMOs post-pandemic will again highlight the industry's capacity constraints as space, resources, and personnel are all in limited supply.

4. The Great CMO Wait

The more than 235 contract manufacturing organizations worldwide aren't enough to meet the anticipated spike in demand for outsourced services, with a 2020 Global Managed Services Report indicating 45 percent of pharmaceutical and medical device companies expect to outsource more in the coming years with the goal of cost savings and faster time to market.[10]

The number of CMO facilities is projected to rise in an effort to fulfill demand and capitalize on market growth. However, it could be quite some time before CMOs can work through the backlog of companies knocking on the door. Challenges to new CMOs entering the market include:

High capital investment: CMOs can expect to spend upwards of $350–400 million to build a new facility equipped with the latest technology and infrastructure.[11]

Lack of skilled professionals: A new facility will require hundreds of skilled biopharma professionals trained in managing complex biomanufacturing processes.[11]

Increasingly complex technology transfer: Protection of intellectual property and quality concerns are leading biopharma companies to consider manufacturing in the United States or Europe as more attractive options than the lower-cost Asian CMO market.[11]

Despite these obstacles, projections indicate total CMO production capacity will increase 60 percent over the next three years in addition to an expanded suite of service offerings, analytic capabilities, and quality enhancements such as continuous manufacturing, perfusion systems, and tangential flow filtration.[6]

While CMOs are currently somewhat of a bottleneck, they are also the industry's best option to catapult new technology into the market at a pace never seen before.

Contract Manufacturing Trends to Watch Over the Next Decade

This decade is off to a wild, unpredictable start that has caused everyone in the biopharma industry to adjust or at least reassess their operations, relationships, and business models.

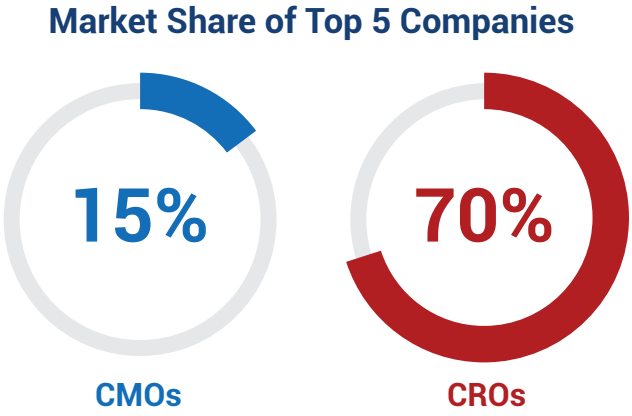
What can the industry look forward to over the remainder of the decade as it relates to contract manufacturing? While many uncertainties still loom, growth seems to be a confident forecast.

1. Greater reliance on outsourcing manufacturing as pharmaceutical and biotechnology companies of all sizes focus on in-house strengths
2. New market entrants to address capacity limitations
3. Increased merger and acquisition activity
4. Greater flexibility in facility design and utilization
5. Continued movement toward Industry 4.0, including artificial intelligence, the Internet of Things, and advanced analytic and modeling technologies
6. Rising prices, though at a slower rate than the past five years
7. Reshoring manufacturing operations and regionalizing supply chains to limit risk, although low prices will continue to draw business to Asian markets
8. Expanded service offerings to build more strategic partnerships

How to Choose a CMO That's Right for You

The good news for biopharma companies looking to partner with a contract manufacturer: There is no dominant market player and there are many organizations from which to choose. The top five CMOs own less than 15 percent market share — in stark contrast to the CRO market where the top five own 70 percent — though this number is expected to shift with rising M&A activity.[12]

The bad news: Capacity remains limited.



Start your CMO search as early as possible and use this list of questions to aid in your discovery and selection process.

1. Does the CMO have the capacity and technology to handle your project?
As we've discussed, capacity limitations will be a critical driver of the CMO selection process. Don't be surprised if your top-choice CMO can't get you in for a year or more.

To help offset this limitation, be prepared with as many specifics as possible so you can capitalize on CMO availability when it's ready for you — it might not last long. Have all your project figures and requirements at your fingertips when engaging with a CMO so you can assess potential fit.

2. Does the CMO's availability match your expected timeline?
Project timelines can vary significantly whether you're producing therapies for clinical trials or ready for commercial manufacturing.

It's wise to engage outside counsel with experience managing complex, end-to-end manufacturing processes to establish a clear, realistic timeline that considers material procurement, quality assurance procedures, records management, product testing, and more.

3. Does the CMO have a process development group?
This is critical to ensuring your technology is suitable to transfer from the R&D phase to manufacturing. Without process development professionals, you run a higher risk of tech transfer issues and delays that you will be on the hook for solving.

When you find a CMO partner with the right process development capabilities, work with them to understand the timeline and scope required to scale up to GMP manufacturing properly.

4. Has the CMO worked with similar products before?
In the world of novel cell and gene therapies, products are becoming more unique and nuanced. Ask your potential CMOs if they have experience manufacturing products like yours, if they have the equipment and analytical instruments required (or if they can procure them), and if they have the right personnel.

5. Does the CMO have everything you will need as you scale up?
Look for a partner that can offer a range of services across different therapeutics instead of selecting multiple partners with niche offerings. Streamlining your partnerships to one or two CMOs will help to simplify your supply chain and minimize disruptions and miscommunications.

Also ask about their redundancy and backup planning in the event a facility or piece of equipment goes out of commission. How will they ensure your production isn't delayed?

As you plan to scale up, can the CMO guarantee availability to service your growing needs? Are they equipped for early-stage production as well as commercial? A flexible facility design will help to alleviate many scale-up concerns.

And finally, ask which functions the CMO handles in-house and which they outsource. Get a list of their outsource partners so you can vet them internally.

6. Does the CMO allow your personnel in the plant?
Some CMOs are very restrictive on whom they allow in the plant. For some companies, that's a dealbreaker. Ask who will be granted access to monitor the manufacturing processes and if there are any limitations to that access. Additionally, access to cameras in the suites will allow you to monitor the processes without being on site.

7. How will the CMO protect your intellectual property?
In an environment where multiple companies discuss and produce highly technical proprietary materials, it's important to feel confident that your IP will be protected. Ask what measures the CMO has in place to ensure privacy.

8. How does the CMO handle lost production?
Read the fine print closely when engaging with a CMO, especially when it comes to lost production time. In the event of lost time or failed batches, are you allowed to be involved in the corrective action and preventive action (CAPA) process to identify the root cause of the loss or failure? And are you welcome to provide input on the CAPA to prevent future failures in quantity and/or yield capacity?

Conclusion

Contract manufacturing is ripe for opportunity, both for the CMOs themselves and for the biotechnology and pharmaceutical companies that choose to use them. Look for the number of CMOs to grow, utilization and productivity numbers to rise, and technology innovations to explode in the years to come.

In Relentless Pursuit of Quality Manufacturing

Whether you manufacture in-house or with a CMO, integrated commissioning and qualification can streamline your schedules and budgets while achieving and maintaining regulatory compliance. Contact biopharma's CQV experts to get it done right the first time.

ICQconsultants.com

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