

2022 Global Pharmaceutical CDMO Outlook

Executive Summary And Outline

Over the past decade, the pharmaceutical sector has increasingly relied on contract development and manufacturing organizations (CDMOs) to support the development of clinical candidates, candidate registration, market authorization and manufacturing. In this second of our two-part series on CDMOs, we will review core areas inflecting growth, the evolving M&A landscape and regulatory considerations that are driving changes in the pharmaceutical CDMO sector. (Please find Part One [here](#), which focuses on Medtech CDMOs.)

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I. Introduction

The value of the partnership between the pharmaceutical sector and CDMOs has been well reflected in the large part CDMOs have played in scaling vaccine production during the COVID-19 pandemic. Outside of COVID-19, 'Big Pharma' has utilized CDMOs to free up investment in manufacturing to help fund pipelines and commercial priorities, while in small and virtual pharma, CDMOs have provided manufacturing capacity and development expertise where little may exist. The pharmaceutical CDMO market has been valued at ~\$90B, growing at ~7% CAGR.¹ Traditionally, investment has been directed at small molecule therapeutics. In recent years, the market share of small molecule treatments has declined while the volume of large molecule and biologic treatments has grown rapidly.

II. Growth in Biologics as a Share of CDMO Operations

In specialized fields like biologics and bioreactor development, CDMOs provide unique expertise that enable 'Big Pharma' and smaller innovators alike to bring products to market more quickly. The global biologics market is approaching a third of the entire pharma market.² Contributing to this trend is not only the continued development of blockbuster biologics (ex., antibody, immunosuppressants, anticancer, atopic dermatitis, etc.), but the rise in the number of biosimilars (identical copies of biologics) being approved as patents continue to expire.

¹ Pharmaceutical Outsourcing Market: Current and Future Strategic Trends. Pharma Tech Outlook: 12/31/2021.

² Marwood meta-analysis of market research in the space

The rise of biologics is evident in the number of CDMOs investing heavily in new biomanufacturing facilities including the biopharmas Fujifilm Diosynth Biotechnologies (\$2B investment), Samsung Biologics' (\$1.7B investment), Lonza (\$935M expansion), Boehringer Ingelheim's (\$827M investment) as well as Therma Fisher and Catalent. This is also reflected in several CDMO transactions in 2021. For example, Danaher acquired the mRNA-focused CDMO Aldevron for \$9.6B and Charles River Laboratories acquired Vigene Biosciences & Cognate BioServices for \$1.2B.

III. Rare Disease a Continued Source of Growth for Small Molecule CDMO Activity

Nowhere is the role of the CDMO more indispensable than in the rare disease space. High-potency active pharmaceutical ingredients (HPAPIs) require specific infrastructure and capabilities, including containment procedures, engineering controls, and personnel handling during development and manufacturing at both clinical and commercial scale. Securing these measures requires a significant capital investment and several years to get a compliant facility up and running. CDMOs that invest in containment procedures and capabilities to handle these types of compounds, we believe, may be better positioned to support the industry and benefit from significant barriers to competitor entry.

IV. COVID-19 Impact

Traditionally operating in the background of the pharmaceutical sector, CDMOs have taken center stage of late as governments around the world demand quick solutions to the pandemic that will involve new medicines and rapid scalability. At the onset of the COVID-19 pandemic, few CDMOs had experience in developing and manufacturing vaccines on a global scale. Most major vaccine manufacturers, including Merck & Co, Sanofi, GlaxoSmithKline (GSK), and Pfizer, along with companies in emerging markets, such as the Serum Institute of India, did most of their development and manufacturing in-house. As the vaccine rollout gained speed, the demand for manufacturing capacity exploded and along with it short, medium and long-term considerations for investors in the sector.

Those lesser-known CDMOs that perform well as vaccine suppliers in the short term, could be given access to more opportunities for higher-value products that would otherwise have gone to one of the very large CDMOs. In the intermediate term, with major pharmaceutical companies consuming bandwidth of the largest CDMOs to vaccines, many small and mid-size injectable CDMOs are building new clinical and commercial capacity to fill a void left by the largest CDMOs, which need big projects to maintain injectable operations. With the pipeline of injectable drugs growing rapidly and record levels of funding flowing to emerging bio/pharma companies, there is a growing need for capacity at the smaller project end of the market. While industry revenue may be getting more consolidated through mergers and acquisitions (M&A), the number of industry participants is actually growing.

In the long term, as the pandemic wanes, a key question with implications to M&A is what will happen with all of the injectables capacity that has been committed to or built for the pandemic response over the past two years? If history is any judge, governments will be challenged to maintain vaccine-preparedness programs that will pay for guaranteed manufacturing capacity for years into the future. Thus, capacity will likely be available at very attractive valuations.

V. Pharmaceutical CDMO Landscape

The CDMO sector has few dominant players (**Figure 1**), with the top players together controlling just under 25% of the market with hundreds of smaller specialists occupying the rest of the market.³ There are now more than 500 CDMOs around the world, each of whom are trying to carve out a specific niche for themselves in certain key markets. The competitive nature of the pharmaceutical CDMO has led to a resistance in consolidation with only a few large players with global reach.

The ability to differentiate services usually comes in one of two ways. The first pathway is a vertically integrated model built around API and excipient manufacturing. Companies partnering with vertically outsourced CDMOs have operations in multiple countries and employ internal teams with deep expertise in compliance, quality assurance, development, manufacturing and materials management to oversee activities of their CDMO partner. These interactions tend to be knowledge-neutral in the sense that both the client and CMO/CDMO have similar levels of expertise.

The second strategy is a virtually outsourced model that centers on performing quality and regulatory services with an acquired API source. Relationships in the virtually outsourced model tend to be weighted toward the CDMO partner in cases where a small virtual manufacturer engages a contract

Figure 1: Leading Pharma CDMOs

Company	Description
AGC Biologics	Asahi Glass first entered the market by acquiring CMC Biologics (now AGC Biologics), a fast-growing biopharmaceutical supplier. AGC Biologics is expanding rapidly across three continents with facilities in the US, Denmark, Germany, and Japan
Boehringer Ingelheim	BioXcellence has one of Europe's largest production plants for biopharmaceuticals (260,000 liters). What's more, the company is a leading contract manufacturer of biologics for 15 out of the top 20 global pharma players
Catalent	Catalent's \$950M acquisition of Cook Pharmica immediately made them one of the top large molecule manufacturers. Its Commercial Mammalian and Microbial Manufacturing business continue to benefit from a robust customer base and strong demand
Lonza	Lonza is a dominant player in the market. Lonza recently expanded into China, partnering with GE Healthcare to bring a biologics facility to Guangzhou in 2020. One of the first to market, Lonza partners with some of the top pharma companies, including a joint venture with Sanofi
ThermoFisher Scientific Patheon	Already one of the largest biopharma CDMOs, Patheon was acquired in 2017 by Thermo Fisher, one of the largest sellers of bioprocessing supplies. Owning a sizable CDMO provides Thermo Fisher with a variety of options for bundling diverse products and services
WuXi Biologics	WuXi Biologics is the dominant leader in China with 63.5% market share and accounts for 35.1% of total revenue. WuXi has made rapid business progress across the US, Europe, and Asia, and its customers include some of the largest global pharma companies
Other Leading Pharma CDMOs	<ul style="list-style-type: none"> • Abbvie Contract Manufacturing • Avid Bioservices • Brammer Bio • Emergent BioSolutions, Eurofins • Fujifilm Diosynth • JHL Biotech • KBI Biopharma • Millipore Sigma • Novasep • Rentschler

³ Marwood Analysis and Frost & Sullivan CDMO Data

manufacturer to manage the entire commercialization process. In some instances, the CDMO serves as a general consultant performing non-core functions, including preparation of documents for the client to submit to authorities, customs and brokerage services and third-party logistics solutions.

The largest CDMOs are particularly attractive to large pharma because they offer broader end-to-end relationships, including large-scale infrastructure and more specialized bioprocessing and regulatory expertise. These CDMOs generally handle all services, from cell line development through fill-finish and packaging. Big Pharma may become increasingly interested in building alliances with large biopharmaceutical CDMOs whether that be through partnerships, joint ventures, or acquisitions. As seen by Thermo Fisher's acquisition of Patheon (\$7.2B; 2017) and \$17.4B acquisition of PPD (2021), a large CDMO can provide a variety of options for combining products and services while maintaining wider control of the value-chain.

VI. M&A Activity

The potential for consolidation in the industry is attracting significant interest from not only private investors, but CDMOs and pharma as well. With so much fragmentation, selecting the right opportunities can be a daunting task. CDMO consolidation has been especially pronounced in the biologics market. Noteworthy activity includes Catalent's acquisition of Paragon (\$1.2B; 2019) and Brammer Bio's sale to Thermo Fisher (2019).

More recently, in 2021, we saw Sanofi agree to effectively become a mega-CDMO in helping Pfizer produce its COVID-19 vaccine, while Bayer and CureVac entered into a multifaceted partnership in order to roll out 160M vaccine doses by 2022. Millipore Sigma, the life science arm of Merck KGaA, acquired German mRNA CDMO AmpTec, pairing AmpTec's PCR-based mRNA technology with Millipore's expertise in lipids manufacturing to strengthen offerings across the mRNA value chain – most notably MilliporeSigma, which is already providing lipids, the central delivery mechanism for mRNA therapeutics, to Pfizer-BioNTech for their COVID-19 vaccines.

On the corporate side, Danaher acquired the mRNA-focused CDMO Aldevron for \$9.6B and Charles River Laboratories acquired Vigene Biosciences & Cognate BioServices for \$1.2B. Looking to add the initial niche capabilities from acquiring small CDMOs followed by additional investments to expand capacity, the WuXi family of companies (WuXi AppTec, WuXi STA and WuXi Biologics) did four deals while three companies – Catalent, Charles River Laboratories, and Resilience – did three each; Thermo Fisher Scientific had two deals in just the first six months of 2021.

CDMO M&A among private equity investors was extremely active in 2021 as they looked to buy their way into the industry and incumbents sought to broaden and deepen their capabilities.

- EQT's \$2.8B Acquisition of Recipharm, a CDMO of APIs and drug products, follows its ownership of the CDMO Aldevron (focused on plasmid DNA for viral vectors) and Fertin Pharma (specialty dose forms); it also owns SHL Medical, a developer and manufacturer of injectable delivery devices
- Partners Group acquired Pharmathen, a European CDMO specializing in advanced drug delivery technologies for complex generic pharmaceutical products, from BC Partners for EUR 1.6B
- NovaQuest Private Equity acquired CoreRx, a CDMO specializing in preformulation, formulation, analytical and stability, clinical manufacturing, commercial manufacturing, and packaging services
- FSNC acquired a majority share in Adragos Pharma Group ("Adragos"), a growing B2B contract developer and manufacturer (CDMO) for pharmaceuticals

VII. Global Regulatory Outlook in the Pharmaceutical Space

Europe

The launch of the Pharmaceutical Strategy for Europe in November 2020 has injected dynamism and the potential for change into the European Union's regulatory environment. Whilst the Strategy will have implications across the medicines market, the big shifts may happen in relation to rare diseases. Mainstreaming orphan drugs within the broader pharmaceutical regulation is under discussion, whilst aligning existing incentives to ensure they push drug development towards where there are clear unmet needs is being considered. Options include reviewing existing exclusivity periods, extending regulatory rewards or introducing a 'voucher' similar to the FDA's pediatric voucher system.

In addition, the EMA explicitly recognizes the value of biosimilars as a way to increase treatment options for patients, and there is a supportive environment for cooperation between EU countries to help incorporate biosimilars into national markets. As part of this drive, EU-level actors may make use of soft policy levers to push for greater biosimilar and generic substitution.

Over 2022, the sector should expect the adoption of a revised Blood, Tissue & Cells (BTC) Directive after it was delayed from the tail-end of 2021. Further progress may be slow, as this is a notoriously sensitive area for Member States, but the impact of Covid-19 on the BTC supply chain may have forced a change in the wider political consciousness.

United States

In the US, the FDA regulatory environment is stable. PDUFA agreements of 2007, 2012, and 2017 helped improve the regulatory environment and the past decade has seen a strong uptick in FDA approvals. The strength in the number of approvals each year is driven by the growing number of NDA filings at FDA. The average number of filings per year between FY2012-FY2017 was 40. However, in FY2018 and FY2019, the number of filings jumped >60% to 64 and 65 per year, respectively. In FY2020, there were a record 73 NMEs filed, which helped drive FDA activity in calendar 2021.⁴

The pace of orphan drug approval has remained stable. The orphan drug program was created under the 1983 Orphan Drug Act to facilitate the development of treatments for rare diseases and grants clinical research subsidies, certain market exclusivities, and tax incentives to products with the designation. Following the announcement of the Orphan Drug Modernization Plan in 2017, to speed review of orphan designation requests, the FDA granted its highest number of approvals with orphan drug designations in 2018 (33 approvals). Since 2018, three out of four years have seen over 50% of drugs approved designated as orphan drugs.⁵

The outlook for biologic drugs that need to be infused or administered by a physician is stable, representing almost one-third of NME approvals each year for the past several years. Since 2014, the number of biologic license applications (BLAs) submitted to the FDA has been in the double digits (with the exception of 2016). Prior to 2014, BLA submissions were in the mid-to-low single digits.

⁴ Marwood Research Note Jan 27, 2022.

⁵ Marwood analysis of FDA.gov: New Drugs at FDA: CDER's New Molecular Entities and New Therapeutic Biological Products Database

VIII. Future Considerations

Marwood continues to follow the regulatory, legislative as well as downstream healthcare payor and provider impacts which may impact developments in the pharma CDMO industry. For example, the UK's involvement in Project Orbis is an attempt to demonstrate regulatory gains as part of the ongoing post-Brexit unwinding. Whilst it is still early days, MHRA approval of AstraZeneca's Tagrisso (osimertinib) in May 2021 offers a glimpse of a potential future of more globalized harmonious drug approvals. CDMOs that are expanding their scope of work may have the opportunity to act as a partner across stages and regulatory frameworks in the product development process.

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