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The State of Outsourced Mammalian and Microbial Capacity

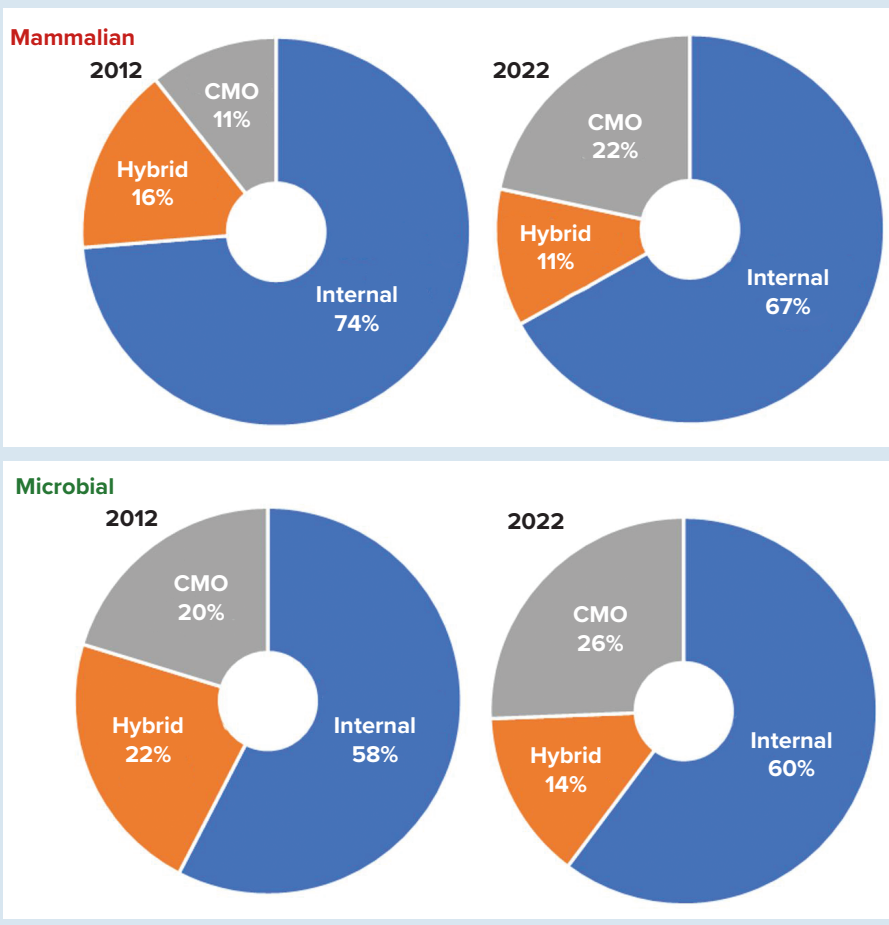
BY DAN STANTON

Recent capacity investments and expansions among contract development and manufacturing organizations (CDMOs) indicate a continuing trend toward outsourcing biopharmaceutical manufacturing. To understand and support capacity expansions and facility acquisitions, biopharmaceutical companies often have used bioTRAK database supply-and-demand reports for impartial, data-driven, real-world analyses. In May 2022, *BioProcess Insider* spoke with Dawn Ecker (managing director of bioTRAK database services at BDO) to learn about developments in manufacturing capacity for bioproduction based on mammalian and microbial cell culture.

Gains for Contract Manufacturers

Over the past decade, the percentage of biopharmaceutical developers with in-house mammalian-cell–culture capacity has decreased, whereas service providers, mainly CDMOs, have doubled their market share (Figure 1). The percentage of "hybrid" manufacturing companies that use capacity for their own product pipelines and as a service to others decreased slightly. On the microbial side of the industry, in-house capacity has stagnated, and the presence

Figure 1: Percentages of bioreactor capacity for mammalian and microbial cell culture held by biopharmaceutical developers manufacturing their own products (internal), contract manufacturing organizations (CMOs), and developers allocating internal capacity for external products (hybrid); statistics from bioTRAK database (**1**)



of dedicated contract manufacturing has grown to the detriment of hybrid capacity.

Ecker and her colleague Patricia Seymour predict that by 2025, CDMOs and hybrid manufacturing companies will control 44% of the estimated 7,500 kL of global mammalian capacity (**1**). Ecker attributes demand for outsourcing of mammalian-cell–based biologics to changes in the mix of products being developed, with pipelines now heavily weighted with monoclonal antibodies (MAbs) and related products. "In 2012," she explained, "40% of the approved mammalian products were antibody based. Today, that is almost 70%." She added that "MAb structure lends itself well as a platform. No matter what the target is, antibodies have pretty much the same structure and size. If you are developing a MAb product, CDMOs and hybrid companies are well versed in a platform manufacturing process, so [today's drug developers] are often comfortable with someone else manufacturing their products."

On the flip side, Ecker continued, "proteins, hormones, and cytokines are all different in size and structure, so those types of products can be a little more challenging to [fit] into a 'standardized' biomanufacturing process." In such cases, developers often prefer to control their own process because third parties might not accommodate the complexities and nuances of their molecules.

Table 1: Contract development and manufacturing organizations (CDMOs) ranked by bioreactor capacity for mammalian cell culture, as listed in the bioTRAK database (**1**); the database notes that 62 other service providers provided mammalian cell-culture capacity in 2012. That number increased to 64 in 2022. (H = "hybrid" company that uses its own capacity to manufacture both internal and external products)

Rank	2012	2022
1	Boehringer Ingelheim (H)	Boehringer Ingelheim (H)
2	Lonza	Samsung Biologics
3	Novartis (H)	Lonza
4	AbbVie (H)	Novartis (H)
5	Merck KgAa (H)	Merck KgAa (H)
6	Human Genome Sciences (H)	WuXi Biologics
7	CMC Biologics	Fujifilm Diosynth
8	Patheon	AbbVie
9	Royal DSM	AGC Biologics
10	Rentschler Biopharma	Thermo Fisher

Table 2: Contract development and manufacturing organizations (CDMOs) ranked by bioreactor capacity for microbial cell culture, as listed in the bioTRAK database (**1**); the database notes that 58 other service providers provided microbial cell-culture capacity in 2012. That number decreased to 51 in 2022. (H = "hybrid" company that uses its own capacity to manufacture both internal and external products)

Rank	2012	2022
1	Novartis (H)	BioVectra
2	Lonza	Lonza
3	Fujifilm Diosynth	Fujifilm Diosynth
4	Pfizer (H)	Novartis (H)
5	Boehringer Ingelheim (H)	Boehringer Ingelheim (H)
6	Merck KgAa (H)	Pfizer (H)
7	Emergent BioSolutions	AGC Biologics
8	Asahi Glass Company Ltd.	Northway Biotech
9	CMC Biologics	Merck KgAa (H)
10	Cambrex	Wacker

Another change over the past decade is a significant increase in the number of companies that have only one or two molecules in their pipelines. For such companies, investing in manufacturing capabilities is neither inexpensive nor speedy. Ecker said, "Companies may view outsourcing their manufacturing as a quicker route to the clinic, and if a molecule does not progress through the clinic, the company is not left owning and staffing — or significantly underutilizing — a facility it no longer needs."

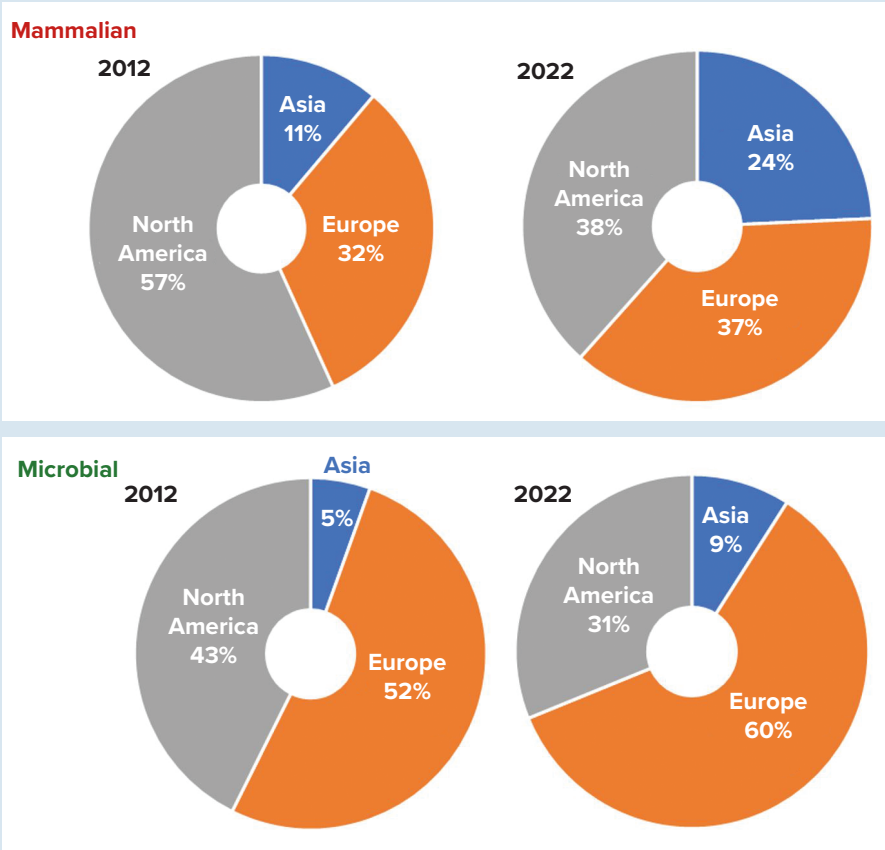
Ecker noted, however, that the trend toward outsourcing differs a bit on the microbial side of the biologics industry, partly because

of its "incredibly diverse" pipelines. "Developing a platform for a microbial product type is not as easy" as it is for mammalian-cell products. "Even if it is a cytokine, enough variations are in the [product] group to limit broad applicability of a single manufacturing and purification process."

Global Distribution of Culture Capacity

Ecker also spoke about the total geographical distribution of mammalian and microbial cell-culture capacity (not differentiating between in-house and third-party capacity) (Figure 2). She explained, "For mammalian [capacity], we have seen Asia increase its capacity holdings since 2012, attributable to several dedicated CMOs and several hybrid manufacturers opening facilities in that region."

Figure 2: Geographical distribution of total bioreactor capacity for mammalian and microbial cell culture; statistics from bioTRAK database (**1**)



In South Korea alone, Samsung Biologics — which was founded in 2011 — boasts three facilities housing 364 kL of mammalian capacity in Songdo, Incheon. A fourth plant with 256 kL of bioreactor capacity will be opening its doors in 2023, and a fifth plant is in the design phase (**2**, **3**). Neighboring Celltrion, which functions both as a drug-program sponsor and CDMO, expects to have 200 kL of mammalian capacity by 2024 and as much as 600 kL by 2030 (**4**).

China, meanwhile, recently reformed laws surrounding its marketing authorisation holder (MAH) system and contract manufacturing operations, helping to drive domestic biologics capacity investment (**5**, **6**). WuXi Biologics has expanded rapidly in China — and elsewhere (**7**). But international CDMOs also have taken advantage of the relaxed regulations, with Lonza and Boehringer Ingelheim recently expanding their capabilities in the country (**8**, **9**).

References

1 Stanton D. Spurred by CDMOs, Global Mammalian Capacity to Reach 7,500 kL by 2025. *BioProcess Insider* 4 November 2021; https://bioprocessintl.com/bioprocess-insider/facilities-capacity/spurred-by-cdmos-global-mammalian-capacity-to-reach-7500kl-by-2025.

2 Stanton D. Despite Pandemic, Samsung Bio Set to Open "Super Plant" Early. *BioProcess Insider* 29 April 2022; https://bioprocessintl.com/bioprocess-insider/despite-pandemic-samsung-bio-set-to-open-super-plant-early.

3 Stanton D. Samsung Biologics Preps to Build Fifth Korean Plant. *BioProcess Insider* 9 November 2021; https://bioprocessintl.com/bioprocess-insider/facilities-capacity/samsung-biologics-preps-to-build-fifth-korean-plant.

4 Stanton D. Celltrion Commits $453m for Third Plant with 60,000 L Capacity." *BioProcess Insider* 19 November 2020; https://bioprocessintl.com/bioprocess-insider/facilities-capacity/celltrion-commits-453m-for-third-plant-with-60000-l-capacity.

5 Macdonald G. China Laws Settle CDMO Status But Leave Regulator Lacking Capacity for Oversight. *BioProcess Insider* 20 September 2020; https://bioprocessintl.com/bioprocess-insider/regulations/china-laws-settle-cdmo-status-but-leave-regulator-lacking-capacity-for-oversight.

6 Stanton D. Chinese CDMO Sector Growing But Unlikely to Make Global Impact. *BioProcess Insider* 26 April 2021; https://bioprocessintl.com/bioprocess-insider/global-markets/chinese-cdmo-sector-growing-but-unlikely-to-make-global-impact.

7 Nelson M. WuXi Bio Grabs Larger Piece of the Bio CDMO Pie. *BioProcess Insider* 24 March 2022; https://bioprocessintl.com/bioprocess-insider/global-markets/wuxi-bio-grabs-larger-piece-of-the-bio-cdmo-pie.

8 Nelson M. Lonza Bulks Up China Offering with Drug Product Plant. *BioProcess Insider* 24 August 2021; https://bioprocessintl.com/bioprocess-insider/facilities-capacity/lonza-bulks-up-china-offering-with-drug-product-plant.

9 Boehringer Expanding China CDMO Plant. *BioProcess Insider* 17 January 2019; https://bioprocessintl.com/bioprocess-insider/global-markets/boehringer-expanding-china-cdmo-plant.

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