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WHITEPAPER

In-house versus outsource: A decision-making guide

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Abstract

The biologics market is shifting its focus from blockbuster drugs to niche markets addressing unmet needs. This now competitive pharma landscape poses challenges to companies may be looking to bring these drugs—that maybe unpredictable and lack stability—to market. Early on, it is wise for companies to examine risks to the molecule's success, discuss issues around capacity, and ensure a smooth regulatory pathway.

An initial key decision would be to keep the process in-house, or to outsource. This whitepaper presents points to be considered in the decision-making process, and in turn, how to choose the best CDMO with the project's future goals top of mind. Larger and more experienced CDMOs like Thermo Fisher Scientific can function as a one-stop-shop with flexible manufacturing strategies. The benefits of outsourcing to the right CDMO include easier scale-up, improved supply forecasting, and the ability to minimize any complications—all resulting in saving time and money.

Introduction

The biologics market is quickly evolving from a focus on developing blockbuster drugs to exploring niche markets with unmet needs. While the changes are exciting, they pose several risks to a molecule's success as competition intensifies, timelines shorten, and capacity challenges emerge. Yesterday's solutions may not be a perfect fit for today's molecules.

Given this backdrop, biopharmaceutical companies are increasingly looking for new strategies to bring biologics to market quickly and cost effectively. Companies must carefully assess whether their in-house teams can truly deliver everything a project needs to be successful from accurate supply forecasting to successful IND submission, to meeting aggressive timelines. In doing so, biopharmaceutical executives must consider how outsourcing fits into their development and production strategy, as well as how to select the best CDMO partner for their business.

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Decision 1: In-house vs. outsource

What are my current internal capabilities?

Don't assume that outsourcing is only a fit for small firms with no resources to manufacture products in-house. Sure, using a CDMO is an absolute "must" for small and virtual biopharmaceutical companies. But the decision for medium-to-large firms to outsource is as much about the company's internal core competencies and capacity as it is about opportunity to optimize the target product as well as the production processes. In addition, companies working with a CDMO can advance several projects simultaneously. Since few molecules actually make it to market, this multicompound development strategy provides more "shots on goal" for the sponsor company.

Experienced CDMOs with the right capabilities can accelerate drug development, streamline scale-up, respond quickly to capacity changes, tap into deep drug and process development expertise, and more. In this manner, using a CDMO can actually become an important part of a de-risking strategy in the biopharmaceuticals world.

"Deciding to outsource is as much about core competencies and capacity as it is optimizing target product and production processes."

How complex is my project, and do I really want to build out a new facility?

For straightforward projects, in-house production work may be worth the investment but only if there are appropriate internal expertise and capabilities. But the reality is, as therapeutic compounds become more complicated with growing interest in antibody-drug conjugates, fusion proteins, glycoengineered mAbs and bispecific mAbs, it's becoming less likely that firms can handle everything in-house.

If in-house work is still on the table, consider the pros and cons of building a new facility. You'll have complete control of an in-house operation and protection of intellectual property. On the other hand, capital costs are higher, timelines are longer—as you must build and validate a new facility—and you'd have to repurpose the equipment if your needs change.

"Some CDMOs specialize in making forecasting far less of an impossible task."

Do I understand the regulatory approval process?

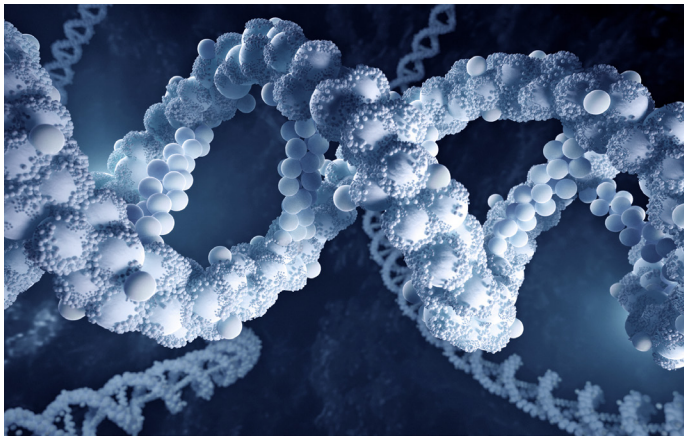
Larger companies that have been through multiple site inspections and product approvals are usually well equipped to handle the regulatory piece of drug development.

On the other hand, small biopharmaceutical companies with a strong research focus—and little regulatory experience—can benefit from a knowledgeable CDMO. Do you have someone to write your INDs? Can you get reports from your manufacturer in eCTD format to make it easier to drop directly into a regulatory document?

If not, consider working with a CDMO that understands how to collect enough CMC data and can build quality into the process at every stage—which is necessary for a smooth regulatory pathway.

Can I forecast my supply accurately and easily adjust if I'm wrong?

In preparation for a product launch, companies need to forecast their production capacity and build their entire process design accordingly. Whether your company is large or small, this is no easy task, since essentially firms are making predictions about a molecule's success well before—often five to ten years—it is on the market. The consequences of underestimating or overestimating supply are costly. Either patients will be without critical medications, or the companies suffer from the expense and wastefulness of an oversupply.



Some CDMOs specialize in making forecasting far less of an impossible task. For instance, when planning for capacity, knowledgeable CDMOs recommend a manufacturer consider both volume and scale to better forecast demand as opposed to simply managing the uncertainty in volume. This approach starts early in the development process with the creation of a target product profile as a tool for determining the API's target cost per gram, the desired cell titer, the proposed dosage regiment and the annual projected production volume.

Skilled CDMOs like Thermo Fisher can draw upon years of experience to assist clients with some of these estimates. From there, the company builds flexibility into the biomanufacturing strategy through techniques such as deployment of single-use technologies, process development and optimization and multiplexing—i.e., where several reactors are linked together in an upstream process to end up with a single downstream process[1].

Decision 2: How do I choose a CDMO?

What are my options?

Biopharmaceutical firms evaluating their CDMO options have numerous possibilities such as big-sized, mid-sized, boutique, single-stop shop or stringing together the offerings of numerous vendors.

Biopharmaceuticals in the discovery/pre-development stage will benefit from using a CDMO with strong development capabilities that can help with cell line development, investigate genes for integration and conduct similar operations.

Smaller CDMOs may be appealing to clients with early-stage projects that have strict budgets and immediate capacity needs. These benefits should be carefully weighed against the resources lost to future tech transfers or if early CMC falls short for ensuring proper scale-up and successful regulatory filings down the road.

Another option for projects in any stage is to partner with larger single-source CDMOs that can work on molecules from pilot through commercial stages. Such as, "one-stop shop" means there's one set of negotiations for one contract and a single project manager overseeing all phases of the project. Singlesource CDMOs usually have broader capabilities, which is helpful as molecules progress toward commercialization and production needs change. Larger CDMOs also minimize the complications and delays from tech transfers as projects move to late-stage and commercialization. Such manufacturers may also help save time and money with flexible manufacturing strategies, easier scale-up and better supply forecasting.

"When considering which manufacturing strategy to choose, the future goals of the project should strongly guide the decision."

Do I need my own cell line?

In the interest of time and ease, some CDMOs will refuse to use external cell lines. If clients transfer out projects from the original CDMO, they're often obligated to pay royalties. Meanwhile, flexible CDMOs will let clients use their own cell lines, tend to have a broader experience with multiple expression systems and are in favor of full transparency. When considering which manufacturing strategy to choose, the future goals of the project should strongly guide the decision.

Can you help me meet aggressive timelines?

When the goal is speed-to-market, the choice in CDMO can be a huge factor. Among the many aspects to nail down are:

- Is immediate capacity available?
- What is the price?
- Do the CDMO's capabilities align with my project?
- Do I need to negotiate multiple contracts?
- Will I need to build in time for tech transfers when my needs "outgrow" the site's capabilities?
- Does the CDMO have development and manufacturing skills/experience and new technologies at all stages that will bring product to the next level?
- Can the CDMO help me accurately forecast clinical supply?
- Is the CDMO's proposed timeline realistic or is it overly-optimistic in hopes of securing the contract?

In the context of efficiency, getting through process validation and product approvals without major road bumps is critical. Using an experienced CDMO is helpful because they have worked with more molecules and can better anticipate hiccups in process design and scale-up. A knowledgeable CDMO will use design of experiments (DoE) techniques during process design to mitigate risks down the road.

Can you help me better forecast supply?

For time and cost reasons, demand forecat accuracy is a critical component in selecting your manufacturing strategy. Today, biopharmaceutical firms need a lot more flexibility. Look for a CDMO with numerous strategies available to respond to supply chaing changes including: single-use systems, scalable technologies, high titer fed batch systems and process development and optimization. Smaller reactors and even multiplexing can also offer a lot of flexibility.

What is the reputation and track record of the CDMO?

What is the reputation of the CDMO? What is their regulatory history? Do they have a fully developed and evolved quality system? What do their quality agreements and confidentially look like? What type of project management do they have? Do they have a core team and sub-teams?

Importantly, will the CDMO use its own internal systems regardless of the customer's needs and preferences? Or, is the CDMO nimble and able to meet the needs of clients of all sizes?

Experienced CDMOs like Thermo Fisher Scientifc firmly believe that restrictive, inflexible operations don't benefit small and emerging clients and continuously look for ways to stay nimble and sensitive to the needs of all clients.

"Biopharmaceutical firms face numerous decisions daily as they address the challenges of bringing biologics drugs to market."

Summary

Biopharmaceutical firms face numerous decisions daily as they address the challenges of bringing biologics drugs—which may be unstable and unpredictable—to market. When selecting the biomanufacturing strategy that is the best fit for their organization, the points considered in this paper are a good starting place for helping you decide whether to outsource and how to best choose the right CDMO partner.

References

1. S. Lam and J. Ward, "Managing Demand Uncertainty in Biologics Production" https://www.patheon.com/en-us/Ideas-in-Action/Material-Details/104/Managing-Demand-Uncertainty-in-Biologics-Production.

About us

Thermo Fisher Scientific provides industry-leading pharma services solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With more than 55 locations around the world, we provide integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vectors, cGMP plasmids, formulation, clinical trials solutions, logistics services and commercial manufacturing and packaging. We give pharma and biotech companies of all sizes instant access to a global network of facilities and technical experts across the Americas, Europe, Asia, and Australia. Our global leadership is built on a reputation for scientific and technical excellence. We offer integrated drug development and clinical services tailored to fit your drug development journey through our Quick to Care™ program. As a leading pharma services provider, we deliver unrivaled quality, reliability, and compliance. Together with our customers, we're rapidly turning pharmaceutical possibilities into realities.

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Dr. Rosenblatt is a subject matter expert in the chemistry and manufacturing controls (CMC) of biotheraputics with a proven 30+ year track record in the biotechnology, pharmaceutical and contracting industries, including positions at Centocor, Johnson and Johnson and Charles River Laboratories. In his various roles with these organizations, he worked with C-level executives on the strategic planning and implementation of organizational initiatives that improved expense to earning ratios (OI). Dr. Rosenblatt currently serves as a CMC consultant to the biopharmaceutical industry covering originator molecules and biosimilars as well as cell therapy. His academic credentials include a BA in Biochemistry from Columbia University, NY and a PhD in Cell Biology/Microbiology/Immunology from the Albert Einstein College of Medicine, NY.

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