Optimizing Your Drug Development Journey: When To Engage a CDMO

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COREALIS Pharma

The drug development process can be long and expensive, so it’s understandable that many biotechs might choose to partner with a contract development and manufacturing organization (CDMO) only when they lack the resources or expertise needed to advance their project. However, waiting too long can backfire, adding unnecessary time and cost.

So … when is the right time to bring a CDMO on board? Understanding your organization’s strengths and weaknesses as they relate to a particular drug development project — and where a CDMO can bring value to each stage — is key.

The Early Stages

Candidate Selection and Pre-Clinical Drug Development

At the onset of a drug development project, you will need to conduct a comprehensive **druggability assessment**, which consists of evaluating the physical, chemical, and biological properties of a compound within the context of a targeted patient population, any dosage requirements, potential regulatory pathways, and a robust IP strategy.

5 Ways a Thorough Assessment Adds Value

When done well, this assessment offers the following benefits to pharmaceutical and biotech companies:

1. Identifying the most suitable structural component of an active pharmaceutical ingredient (API)
2. Developing a strategy for the first-in-human (FIH) and later-stage clinical studies to accelerate timelines, reduce costs, maximize IP, and increase the market value of the drug
3. Creating a robust drug product CMC (chemistry, manufacturing, and controls) package to streamline licensing agreements and regulatory approval
4. Facilitating fundraising by providing **drug proof of concept** (POC) data to potential investors
5. Preventing potential deal-breakers or financial discounts resulting from uncertainties around potential additional drug product formulation development, clinical supply manufacturing, and other associated risks

How Going it Alone at This Stage Can Backfire

You have no doubt seen this statistic before: **90% of clinical trials fail**. The statistic is accurate, but it's become so widely accepted that it's seen as an unfortunate but unavoidable aspect of drug development. However, we've spoken with a number of senior scientists from large pharmaceutical companies, and what they told us was even more sobering:

- Only 2% of all biotech companies are adequately executing sound drug product formulation development
- Inadequate drug product CMC packages are a major cause of deal failure or value erosion

Of course, that's our data. But these findings are in line with a few other stats we didn't originate. **30% of drug development projects** are terminated due to unforeseen toxicity, **40-50% fail** due to a lack of clinical efficacy, and another 10% fail due to a lack of commercial needs and poor strategic planning.

In short, many drug development failures are entirely preventable with proper formulation. But that's not where many biotechs are investing their resources, and that produces a few very common — and often very expensive — outcomes.

7 Ways Poor Drug Formulation Can Ultimately Erode Value

While the drug development process will never be without risk, here are a few examples of what can result from improper formulation or a poorly documented manufacturing process:

1. Having to initiate new stability studies with uncertain outcomes
2. Failing to optimize a key property of your compound, leading to an inappropriate pharmacokinetic profile in humans
3. Finding lot-to-lot variability in API attributes (e.g. changes in polymorphic forms)
4. Needing additional analytical methods or qualifications
5. Having to conduct additional clinical studies when using different drug product formulations, which may subsequently reveal changes in pharmacokinetic profiles
6. Facing challenges in manufacturing scalability for submission batches and subsequent commercial production
7. Experiencing delays in regulatory approvals and commercialization

Considering the many problems that cutting corners can cause, it might be surprising to an outsider that many biotech companies choose to do so at this stage. After all, the cost of failing to invest in **proper formulation** is often in the hundreds of millions of dollars. Venture capitalists who aren't paying proper attention to a drug CMC package can also stand to lose millions if not billions.

Unfortunately, biotech companies often remain unaware of the root cause of their failure.

3 Reasons Poor Formulation Remains Commonplace

Where you have widespread failures, you likely have systemic issues. That's certainly true in our industry around the world.

/ Biotechs Don't Know What They Don't Know

The scientists responsible for drug development often lack the specific expertise required to build and conduct a suitable formulation development program. They often originate from other pharmaceutical development sectors or academia and are placed in their roles by administrators who also don't understand what it takes to fulfill such a position.

Some of these scientists, to their credit, will know enough to bring in a consultant. But they will have the same difficulty — lacking the necessary expertise to select a qualified candidate.

/ Those Who Know Don't Tell

Regulatory authorities such as the FDA, Health Canada, and the European Medicines Evaluation Agency (EMEA) are focused on ensuring that sponsors adhere to the ICH good manufacturing practice (GMP) guidelines. They don't tend to provide feedback to pharmaceutical and biotech companies on the appropriateness of their formulations.

/ The Absence of a "No" Is Interpreted as a Yes

Biotechs often misinterpret this lack of feedback as indicating that their drug product formulation isn't important, and will move into clinical trials with a drug product that is already doomed to fail.

Clinical Development

Navigating Supply and Compliance Issues

Meticulous drug formulation doesn’t ensure a successful commercial product, but it dramatically increases the odds. So, too, does expertise in the clinical trial stage.

Here’s why …

During a clinical trial, a biotech is tasked with proving that its investigational medicinal product (IMP) — commonly referred to as the study medication — is safe and effective, and that the manufacturing process is consistent and valid. Selecting a phase-appropriate drug product formulation at every clinical trial phase and manufacturing that formulation according to GMP requirements is key.

So, without getting too into the weeds, let’s briefly explore a bit more about the clinical supply requirements associated with each phase.

Phase I

Clinical Trials

In this phase, the IMP should have undergone just enough formulation development efforts to provide sufficient exposure in healthy volunteers to complete single ascending dose (SAD) and multiple ascending dose (MAD) studies to establish safety.

Phase II — Early Phase III

Clinical Trials

Here, the IMP should be optimized successfully to ensure that it will be acceptable to the targeted patient population, has the required shelf-life stability, and is able to be successfully manufactured at scale.

Late Phase III

Trials

During late Phase III trials, the formulation and manufacturing processes will be locked, and submission batches will undergo a full validation for NDA submission.

The Advantages of Working With a CDMO Skilled in Clinical Trial Supply and Regulatory Compliance

A CDMO is tasked with keeping up with multi-national regulatory trends and issues that can affect drug products. That's no small feat, and entails continuous vigilance and relying on **internal quality practices** as well as independent audits in order to anticipate how certain evolving requirements may affect current and future projects.

Therefore, a highly skilled CDMO can offer a number of possible advantages that can be worth far more than the costs associated with partnership:

- Increasing the odds of regulatory approval
- Reaching the market faster than any competitors
- Securing a lucrative deal with a larger pharmaceutical company
- Providing regulatory agencies with robust data that can support product claims or submissions
- Being able to adapt to any last-minute changes to supply requirements or last-minute requests
- Attracting additional funding at this stage in the process
- Being able to seamlessly transfer technology and protocols to commercial manufacturers

Common Clinical Trial Supply Missteps

You can probably anticipate many of these, or perhaps you've experienced some of them.

Not Adjusting Formulations at the Right Time

Believe it or not, some biotechs have used Phase I drug product formulations in Phase II and III studies. Unfortunately, failing to select phase-appropriate formulations can cause serious setbacks. For example, if the formulation needs to be changed after the fact, additional clinical bridging studies may be required to show the equivalence of the old formulation with the new one in order to utilize previous clinical data.

Failing To Meet Supply Commitments

Noncompliant GMP operation or documentation, or even minor delays in product development, manufacturing, or distribution can lead to delayed regulatory approval for commercialization. A delayed approval process can subsequently cause lost income, lost deals, and, ultimately, lost opportunities for patients in need of life-saving medication.

Common missteps with drug formulation and clinical trial processes contribute significantly to the high rates of drug development failures. But those aren't the only areas that introduce risk.

Avoiding Scale-Up Challenges
in Commercial Drug Manufacturing

Some biotechs assume that working with a full-service CDMO will eliminate any scale-up issues. However, considering that flawed formulation and clinical supply manufacturing processes pose a greater risk to profits down the road, this assumption may not serve them well for more complex projects.

Any niche CDMO with a proven track record of facilitating successful commercial launches will — by necessity — have also perfected successful technical transfers. If you're vetting this skill set, ask a potential CDMO if they customize their tech transfers according to the capabilities and equipment of the receiving site.

The Importance of Pharmaceutical Technical Transfer

It’s very possible that a CDMO tasked with transferring not only the process of manufacturing the drug product, but also key knowledge and records, may be delivering these items to one of their competitors for other projects. Providing a competitor with the same meticulous attention to detail and care they’d like to receive requires a culture that prioritizes the long-term success of a project above all else.

In other industries, that may be a tall order, but here, it’s non-negotiable.

Given the complexity of pharmaceutical manufacturing, even small discrepancies during transfer can have significant impacts. When done well, a technical transfer can help:

- Assure the product’s consistent quality, efficacy, and safety
- Minimize delays in production
- Avoid unnecessary expenses and waste
- Support regulatory submissions and approvals
- Preserve and communicate critical knowledge about the product and its processes
- Protect proprietary information
- Mitigate potential supply chain issues
- Reduce the risk of product shortages or recalls

What Can Happen to the Best Laid Plans?

Even with excellent formulation, an impeccable clinical trial process, regulatory approval, and all of the information needed to produce a successful commercial product at scale, it’s still possible for something to go wrong.

A receiving site could modify the formulation, the manufacturing process, or the operating conditions without consulting the information provided — therefore introducing an entirely new set of risks at the final stage of drug development.

In fact, this has actually happened more than once … which is why it’s vital to choose the right partners at every stage of the drug development journey. Some CDMOs — Corealis included — can fix problems that occur even after a project leaves their hands by, for example, providing additional assistance to a receiving site as well as conducting small-scale experiments to help adjust the formulation or manufacturing processes as needed.

But depending on the partner you choose, this may not be possible.

How and When To Choose the

Best CDMO Partner

The “right” CDMO partner for any particular project will provide the right expertise needed at the right stage of development to best reduce risk throughout the process. That means the CDMO that offers the potential for the highest rewards is not necessarily the CDMO submitting the cheapest bid.

If you’ve been involved in drug development for quite some time, and you are frustrated by repeated setbacks, missed deadlines, and unexpected costs, it’s likely that you either haven’t partnered with the right CDMOs or haven’t partnered with them soon enough in the formulation stage to catch small issues before they cause catastrophic problems.

Work Your Contacts

Fortunately, there's no need to become an expert in every aspect of drug formulation in order to choose a CDMO wisely. You just need to ask around. The global pharmaceutical industry is, in many ways, a very small town. Large pharmaceutical companies have witnessed what can and often does go wrong in drug development, and it's their business to know which CDMOs consistently produce quality results they can trust.

Start Potential Partnership Conversations Early

It's easy for us to say this, but from our vantage point, it's also easy for us to see it clearly: The most successful drug development programs typically involve engaging a skilled CDMO as early as possible. Ideally, this would happen as soon as the pharmaceutical or biotech company has selected a lead candidate and is preparing to gather pharmacology and toxicology data.

Not only can an early partnership increase the likelihood of saving time and money as well as protecting your intellectual property, but some partners will also offer additional benefits that can more than offset any additional costs associated with a longer-term partnership.

For example, at Corealis, we offer complimentary **Druggability Assessments** to assist with this next step of the process, which can inform a strategic formulation development plan. We also can help biotechs develop the type of robust drug product CMC package that can attract additional investments and negotiate more attractive deals.

/ Visit a CDMO On-Site

Beyond what's listed on their website, make sure that any potential partner has the **state-of-the-art equipment** needed for your project. Additionally, every instrument and every piece of equipment should be well-maintained, calibrated, and thoroughly cleaned in order to ensure that every manufacturing program will ultimately meet the rigorous standards of ICH-GMP requirements.

An excellent CDMO should be enthusiastic about **scheduling a visit**. Be wary of one who isn't.

/ Don't Overlook Culture

Poor communication, a lack of respect, and a hesitance to tell the truth should be deal-breakers. Get a feel for a **CDMO's culture** before you sign anything.

It's hard for some CDMOs to be able to bring bad news to a client, especially when it may threaten a potentially profitable project for them. At Corealis, we understand that preserving the relationship is more important than any potential short-term rewards.

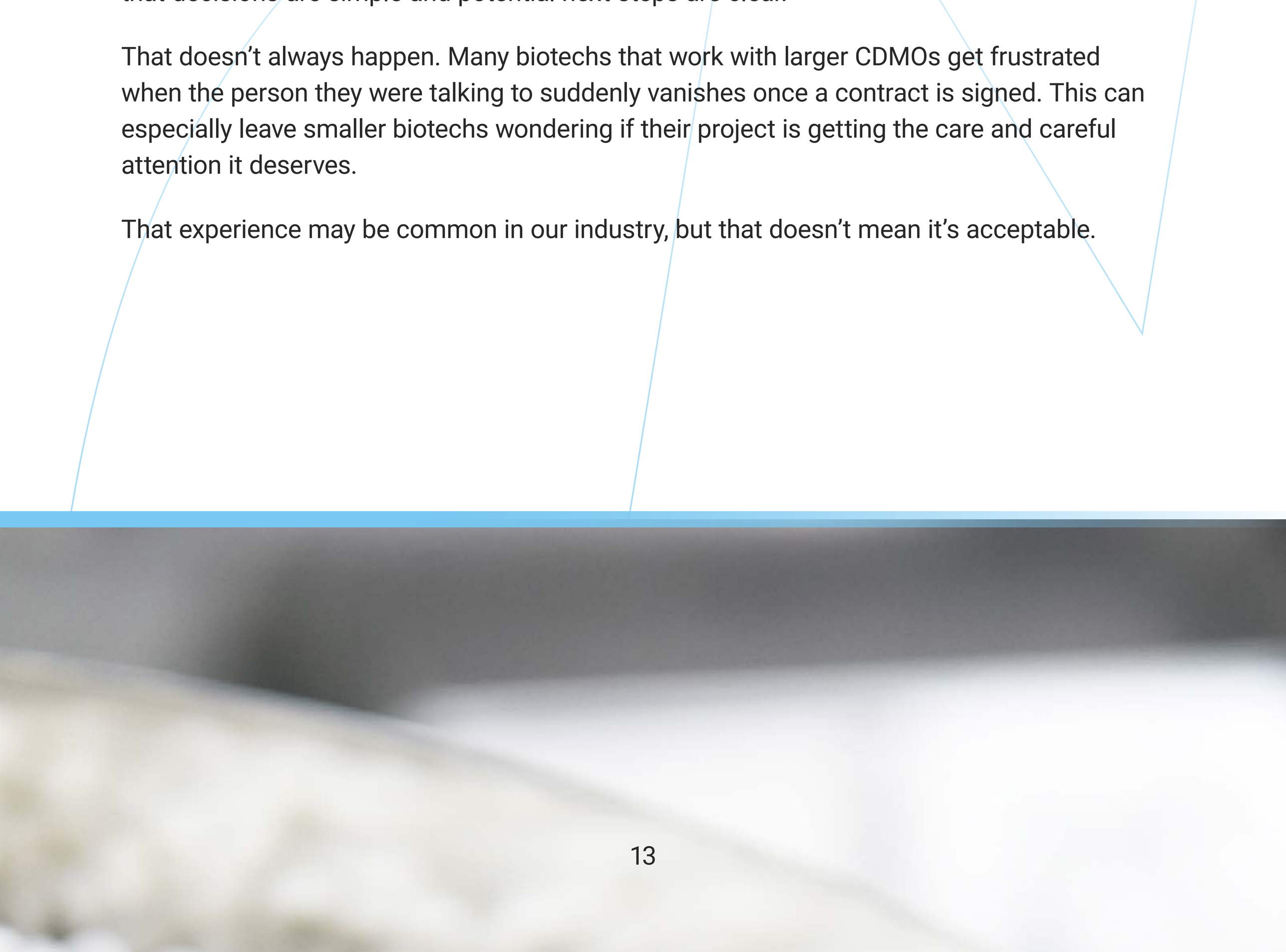
/ Discuss How You Will Communicate

No two clients or projects are entirely the same, and your CDMO should offer you some flexibility to adapt to the needs of your team.

At Corealis, our clients select the frequency of their regular meetings. We also **aren't big enough to have a "B" team**. Our clients communicate directly with the scientists and project managers involved in their process and are kept informed about the latest developments so that decisions are simple and potential next steps are clear.

That doesn't always happen. Many biotechs that work with larger CDMOs get frustrated when the person they were talking to suddenly vanishes once a contract is signed. This can especially leave smaller biotechs wondering if their project is getting the care and careful attention it deserves.

That experience may be common in our industry, but that doesn't mean it's acceptable.



Have an Upcoming Oral Solid Dosage (OSD) Project?

At Corealis, we don’t do everything. But what we do, we do very well. If you anticipate needing the services of a CDMO for an upcoming OSD project, we should talk!

You’re welcome to connect with us at an **upcoming industry event**, or visit our facility in Laval, Quebec at a time that works best for you.

BOOK A MEETING