CASE STUDY Elementary CMC & Pharmagro

BIOTECH & CMC STRATEGY

Choosing the Right Manufacturing Partner for a Phase 3 Biologic

How we navigated compounding process changes, non-comparable proposals, and hidden CDMO risks.

Sector: Biotech / CMC & Manufacturing Strategy | **Engagement:** CDMO selection for Phase 3 and commercial biologics manufacturing

The situation

Our client, a clinical-stage biotech, was developing a monoclonal antibody for an inflammatory skin condition. The program was approaching the end of Phase 2b, with a decision that couldn't wait for the readout: who would manufacture the Phase 3 material, and could that same partner realistically carry it through to commercial launch at the required scale.

The client wanted to incorporate three significant improvements between Phase 2 and Phase 3 production:

- **Increase drug substance concentration by 50%**
- **Increase the drug substance scale significantly**
- **Change the drug product presentation from a lyophilised vial to a pre-filled syringe**

Each change would have significant implications for demonstrating comparability, generating necessary stability data, and ensuring the regulatory pathway remained clear and defensible to both FDA and EMA — particularly given the compounding risk of introducing more than one change to the same Phase 3 programme simultaneously.

The chosen CDMO would need a strong technical team to deliver this on time. Two manufacturing organisations submitted proposals. On paper, both looked credible. But neither proposal, as submitted, was comparable to the other.

What we were asked to do

Run the CDMO selection process end to end: structure the evaluation, interrogate both proposals technically and financially, surface the risks neither vendor was going to volunteer, and land the client on a recommendation they could defend to their board.

We split the evaluation into two lenses that neither proposal provided on its own: what's actually needed to get through Phase 3, and what's needed for BLA readiness and commercial supply. Vendors tend to quote these together, which makes early-stage decisions look more expensive and more urgent than they are. Separating them let us weight the Phase 3-critical items properly and stop early capital from being spent de-risking commercial-scale questions that were still years away.

From there we ran a six-step process:

1. Compliance screening against the client's mandatory timeline
2. Technical and process fit assessment, particularly around the formulation and presentation changes
3. Financial evaluation with cost items standardised across vendors
4. Vendor risk assessment covering everything from inspection history to project team turnover
5. Formal Q&A round to chase down the gaps both proposals left open
6. A weighted scoring matrix to bring it all together

What we found that wasn't in either proposal

⚠ A DP capacity gap hiding in plain sight

One vendor's proposed US site could fill 10,000 units of drug product per batch. The client's Phase 3 demand easily exceeded that. The proposal didn't flag this. Upon further interrogation, the vendor proposed to manufacture the drug product at a completely different site on another continent.

The client wanted to keep production in the US, leaving us to recommend that the client build a contingency position with a second fill/finish supplier who had US capacity from day one.

🌐 A geopolitical risk with a real date attached

One of the vendors was at risk of being added to the US government's "companies of concern" within six months, followed by a safe harbour period. We mapped that against the client's planned US launch date and found the safe harbour window would still be open.

This was not a reason to rule the vendor out — their proposal was genuinely stronger in several areas — but it was a reason to have a funded fallback plan rather than a single point of failure.

Costs that weren't actually comparable

When we itemised both proposals down to the same categories, one vendor's stability programme stopped well short of what the client would need for a BLA-supporting dataset. Rather than flag it as a gap and move on, we modelled out what the missing stability timepoints would actually cost if run to the required 36 months. We also separately costed the raw material and consumables delta from switching to that vendor's platform materials.

Both numbers were substantial, and both were absent from the vendor's headline price. Comparing the two proposals on their stated totals alone would have understated the true cost of one of them by a meaningful margin.

A scale decision the client hadn't stress-tested

Both vendors had priced options at larger manufacturing scale, on the logic that bigger now avoids a second technology transfer and scale-up later. We ran the actual demand numbers: at the proposed scale, a single batch produces enough drug substance to cover the entire Phase 3 programme with material to spare. The commercial forecast would take some time to meet peak demand, meaning PPQ material would likely also be in excess.

The consideration of what to do with excess DS material was brought into scope, making the client aware that storage costs, material expiry, and shelf life all need to be factored into overall cost evaluation when selecting the DS scale.

Funding the programme against the odds of it actually happening

Phase 2 to Phase 3 transition failure is common enough that it belongs in a manufacturing budget conversation, not just a clinical one. We used published industry base rates for transition probability at each phase and translated them into a two-stage funding structure for the client: a defined spending ceiling to get through to the Phase 2 readout, and a separate, larger ceiling that only gets committed once that data is in hand.

It gave the client's finance team a framework for capital release that was tied to actual risk retirement points in the programme, rather than a single upfront commitment sized for the best-case outcome.

The outcome

The client selected a manufacturing partner with a clear-eyed view of where that partner was strong, where the real risks sat, and what a fallback position would look like if one of those risks materialised.

> *Both proposals, once standardised, showed a credible path to being ready to dose Phase 3 patients on the same timeline — which meant the final decision could be made on technical fit, risk, and true comparable cost, rather than on whichever proposal happened to look cheaper on the cover page.*