

Zero Questions: A Phase 2 IND, Two Tech Transfers, and a 10-Person Biotech

How Syner-G's integrated CMC, quality, and regulatory team carried a lean U.S. biotech company through dual global tech transfers, process intensification, and an FDA IND submission that came back without a single agency question.

Background

A U.S.-based biotech with fewer than ten employees was preparing to move its lead biologic into Phase 2 clinical trials. The next step required a new IND to support a new indication and, simultaneously, a near-complete rebuild of the supply chain behind it: a new drug substance (DS) CDMO in Europe, a new drug product (DP) CDMO in the United States, a meaningfully updated DS process, and a redesigned DP presentation.

Internally, the company had strong scientific leadership but lacked the operational bandwidth required to orchestrate this demanding and multifaceted transition. They needed an integrated partner who could assume leadership over the technical work, quality oversight, and regulatory authoring in parallel, ensuring every workstream produced a flawless IND dossier for FDA review.

The Challenge

The client had to execute, in one engagement, a highly complex program that most organizations sequence over multiple years. With a 10-person internal team, any operational or communication gap between technical, quality and regulatory execution would translate directly into program delays or regulatory risks.

The critical complexities included:

- **Technical and Process Intensification:** Transferring the CHO-based DS manufacturing to a European CMO at 1,000 L scale, while simultaneously transitioning the process from fed-batch to perfusion, introducing a new capture resin, and advancing a high-concentration formulation.
- **Delivery Presentation Redesign:** DP manufacturing transfer to a U.S. CDMO into a 2 mL prefilled syringe (PFS), which demanded complex mixing studies for thawed DS pool, and a revised sterile filtration strategy following a critical filter change.
- **Logistics and Infrastructure:** Managing analytical method transfers, comparability and stability studies, and a reference standard strategy distributed across multiple international laboratories, all while maintaining full quality oversight and data verification on an aggressive Phase 2 timeline.

The Syner-G Solution

Syner-G deployed an integrated, cross-functional team that operated as a true extension of the client's organization, covering CMC, technical operations, quality assurance, and regulatory authoring under a single program leadership model. By eliminating traditional consultant silos, the team led high-level strategy while owning day-to-day execution, proactive risk management, real-time decision-making during manufacturing, and continuous CDMO oversight.

IND Authored to
Submission: ~2 Months

0 FDA Questions on the
IND Submission

2 Concurrent Tech
Transfers (DS to
Europe, DP to U.S.)

1,000 L CHO DS Process

10-Person Client Team

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Case Study

Technical Operations and CMC Execution: On the technical side, Syner-G owned end-to-end execution across both DS and DP. The team managed the DS tech transfer to the European CDMO and the DP tech transfer, including labeling and packaging, to the U.S. CDMO. Person-in-plant (PIP) coverage was deployed on the manufacturing floor to ensure execution fidelity during critical manufacturing windows.

Analytical activities, including method transfer, comparability, stability, and reference standard strategies across multiple labs were coordinated alongside the global logistics required to keep samples and materials moving on schedule. Crucially, the team evaluated existing GMP material against historical and ongoing stability data to support re-release and expiry extension. This maximized the client's prior capital investment, preserving valuable inventory and eliminating unnecessary cost and timeline risks.

Integrated Quality Assurance and Regulatory Authoring: In parallel, Syner-G served as the client's quality function. The team prepared and approved vendor quality agreements; reviewed and approved specifications, batch records, analytical data, and release documentation; led vendor audits, and managed deviations, investigations, and CAPAs. Change control around the CDMO transitions and process updates was owned by Syner-G, as were analytical method validation and verification reviews, internal SOP generation and maintenance, and quality documentation. To maintain tight timelines at the European DS CDMO, the Syner-G managed the real-time transition and technical review of critical batch records selection, preventing typical cross-border QA release delays.

On the regulatory side, Syner-G authored Module 3 of the IND in parallel with active manufacturing and data generation. The tightly integrated approach enabled the team to conduct comprehensive data verification across all sections in real time, ensuring the CMC, analytical and quality content reached the FDA clear, consistent and perfectly aligned with agency expectations upon batch completion.

Real-Time Technical Problem Solving: Several technical issues that surfaced during execution were resolved rapidly without slippage of the program timeline:

- **Bioreactor Yield Optimization:** A bioreactor change associated with the DS transfer affected oxygen transfer and yield; Syner-G led the troubleshooting and implemented adjustments to oxygen transfer controls during GMP runs, restoring process performance.
- **Assay Interference Resolution:** Invalid results in the compendial mycoplasma liquid/solid medium assay for the bulk harvest pool were generated due to matrix interference, Syner-G helped resolve the bottleneck by supporting a transition to a validated, regulatory compliant qPCR-based method that delivered reliable detection.
- **Defensible Filter Strategy:** When the DP sterile filter change called validation timeline/strategy into question, Syner-G executed and documented a rigorous technical risk assessment that justified deferring full validation until Process Performance Qualification (PPQ), avoiding unnecessary delay while keeping the filing regulatorily defensible.

Outcomes

The program met its Phase 2 enablement goal without compromising on quality or compliance:

Rapid Parallel Execution: Module 3 authoring kicked off in May alongside active manufacturing, analytical, and quality workstreams, culminating in an IND submission to the FDA in July, roughly two months later, with no schedule slip.

Supply Chain Established and Managed: Both global technology transfers were completed successfully, with engineering and multiple GMP runs executed to support Phase 2 clinical supply. PIP coverage on critical campaigns kept issue resolution real-time and execution reliability high.

Inventory Maximized: Evaluation of historic GMP lots successfully supported expiry extensions, pulling significant cost and timeline risks out of the program.

Zero FDA Questions: The submission returned zero questions from the FDA, a clean reflection of the technical strength of the underlying CMC, analytical, and quality work, and the precision of the Module 3 authoring.

A sub-ten-person internal team ran a complex global program end-to-end, with Syner-G absorbing the operational burden and lifting the bar on execution quality and regulatory readiness.

Conclusion

Small biotech companies do not need a large internal organization to advance complex, intensified programs into Phase 2; they need the right external partner running technical execution, quality, and regulatory authoring as a single connected workstream. Syner-G's integrated model is built for that scenario. When deep CMC expertise, full QA ownership across global CDMOs, and strategic regulatory authoring sit on a single team, lean clients move through critical milestones with absolute confidence, and as demonstrated in this program, resulting in a IND that moves through the FDA with no questions at all.