



## CASE STUDY

# From Clinical Hold to Approval: Overcoming CMC Challenges to Achieve Priority Review and BLA Approval

A clinical-stage biotechnology company encountered a significant regulatory setback during pivotal Phase 3 development when a major change to a critical raw material supplier resulted in a partial clinical hold from the FDA. While the company was able to complete clinical trials using pre-change material, it faced increasing urgency to resolve the Agency's concerns and establish a viable path to incorporate the new material into commercial production. Compounding this challenge was a period of limited FDA interaction, creating uncertainty around regulatory expectations ahead of BLA submission.



ProPharma's Regulatory Sciences team was engaged to provide strategic leadership and reestablish effective communication with the FDA. Acting as the authorized representative, the team rebuilt Agency engagement, developed a comprehensive response to address comparability and safety concerns, and successfully secured a lift of the clinical hold within 30 days.

Beyond immediate issue resolution, ProPharma guided the development of a robust CMC and regulatory strategy to support BLA submission and long-term commercialization. Through proactive planning, high-quality submissions, and continuous FDA engagement, Company A achieved BLA acceptance, priority review, and ultimately approval—enabling timely patient access to a much-needed therapy while strengthening its regulatory position for future success.

## challenge

During ongoing Phase 3 trials, the client implemented a major CMC change involving a new supplier for a critical raw material. FDA did not accept the initial comparability and safety assessment, resulting in a partial clinical hold on the post-change product in clinical studies.

While the company was able to complete trials using pre-change material, **the organization faced several urgent challenges:**

- **Addressing FDA concerns related to comparability and safety**
- **Lifting the partial clinical hold to enable future development**
- **Aligning on a viable path to use the new raw material for commercial production**
- **Reestablishing effective communication with the FDA after a period of limited interaction**
- **Preparing a robust and defensible CMC strategy for BLA submission**

## solution

Our team reestablished communication with FDA, serving as the authorized representative and building a strong relationship with the Regulatory Project Manager. This enabled productive dialogue and a clear path to resolution.

**A comprehensive response to the clinical hold was developed and submitted, resulting in the hold being lifted within 30 days. Our team then led development of the CMC and regulatory strategy, including preparation for a Type C meeting and design of a robust comparability and bridging program. This included analytical methods bridging, process and product comparability, and plans for validation, release testing, and stability—all aligned with FDA expectations at the pre-BLA meeting.**

The team also developed a high-quality briefing package and strategic questions that clarified FDA expectations and areas of flexibility, enabling efficient BLA authoring. Following submission, we supported all regulatory interactions, including information requests and key review milestones, while maintaining ongoing communication with the Agency to ensure alignment.

In parallel, ProPharma supported inspection readiness through a proactive mock audit and preparation for the Pre-License Inspection, including development of key quality documentation.

## outcome

Our client successfully overcame a complex regulatory challenge and advanced to approval. The partial clinical hold was lifted within 30 days, and alignment with FDA enabled use of the new raw material for commercial production.

**The BLA was accepted with priority review, and the review process proceeded efficiently due to strong preparation and timely responses. The company successfully navigated inspection activities and ultimately achieved full BLA approval.**

This outcome not only enabled patient access to a therapy addressing an unmet need, but also strengthened the company's relationship with FDA and positioned it for continued regulatory success.

**“ProPharma’s experience, patience, guidance and assistance throughout the whole process was what led us to this approval. We were very impressed on the professionalism that the whole Regulatory Sciences team carried themselves throughout this process.”**