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Executive Summary

Drug development is filled with critical regulatory moments that can either propel a program forward or bring it to a halt. The path to approval is theoretically well-charted, but real-world examples reveal how strategic sponsors leverage key milestones to accelerate timelines and optimize outcomes.

The FDA is undergoing significant transitions, with workforce restructuring affecting approximately 19% of staff and key leadership changes, including the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research.[1]

Matthew Weinberg, President, Regulatory Sciences, ProPharma, has watched the evolution of the FDA over his nearly 40 years in regulatory consulting. "Change happens all the time. FDA, however, has always been a relative constant," he said. "[Now], science and politics are more intertwined than ever."

While these changes create new dynamics, experienced sponsors can adapt by doubling down on proven strategies like strategic planning and proactive engagement, especially around major moments in the development lifecycle.

Several regulatory milestones are critical for program success, but they may not be the ones that come to mind first.

THE MOST CRITICAL REGULATORY MILESTONES

A few ideas immediately jump to the forefront when thinking of make-or-break moments in drug development. Submitting an Investigational New Drug (IND) application or submitting a New Drug or Biologics License Application (NDA/BLA) seems an obvious choice. Yet, Weinberg says it's a meeting sponsors don't pay enough attention to that could cost them dearly: the End of Phase 2 meeting.

End Of Phase II
Typically occurring between 18-36 months before submitting an NDA, the End of Phase 2 meeting has sponsors solidify their approach and present critical clinical findings to the FDA. It answers the questions of what data and how much more money is needed to finish development. When done correctly, this meeting represents perhaps the most strategic opportunity for sponsors to solidify their regulatory pathway.

"I think most companies don't take that with the seriousness that we have learned over the decades it deserves," said Weinberg.

Recent high-profile CRLs have highlighted how missed opportunities during key regulatory milestones—from inadequate safety packages to overlooked chemistry, manufacturing, and controls (cmc) details—can cost sponsors years and millions in delays.[2]

Sometimes regulatory thinking evolves, and the FDA may request additional toxicology data or clinical information. A sponsor may have to schedule two end of Phase II meetings because they are responding to a particular issue raised during the first meeting. Speed bumps like this happen, but finding common ground with regulators is essential.

The most successful sponsors view these moments as an opportunity for dialogue rather than an obstacle. The goal is to emerge from this milestone with a development plan that's fully aligned with FDA's expectations and is positioned for success.

First Impressions And Final Checks
Critical moments in the regulatory process also come before the big milestones.

The pre-IND meeting, for example, doesn't always get the attention it deserves. This is the day that sponsors appear in a formal capacity to tell regulators about their plans.

"I've been telling clients this for years: this is the first time in general the FDA sees you," said Weinberg. "And I've always thought they make an assessment that says, 'okay, these guys know what they're doing' or 'they don't know what they're doing'."

The pre-NDA meeting also holds significance because it's the last chance to confirm that a sponsor has all the data they need and that everyone, including regulators, is on the same page. While this milestone seems less important compared to earlier critical junctures, it is far from trivial.

The pre-IND and pre-NDA meetings are the FDA's first impressions and final checks. These are the times to ensure everything is in alignment before a sponsor submits their application. If handled correctly, pre-planning meetings can set sponsors up well for application submission.

HOW SPONSORS CAN SUCCEED

The regulatory process can be long, slow, and costly. Many small- to mid-sized drug developers are looking for an edge—a way to speed up the process and minimize cost. The best optimizers may lie in strategic planning and working with experienced thought partners to create the most effective approach.

Leverage Expert Guidance To Partner With Regulators
Never underestimate the amount of data the FDA will need to determine if a treatment is safe. "FDA's mandate is to protect the American people," he said, "They're always thorough on the toxicology data," said Weinberg.

He has seen programs derailed because toxicology data didn't receive enough attention. Better communication between toxicology and clinical departments and analytical thinking in earlier stages could help prevent such headaches.

Sponsors should also seriously consider having a consultant assist in the regulatory process. While the temptation to save money by skipping consulting fees and interacting with regulators directly is strong, that can backfire more often than not. Consultants know that the most successful sponsors don't treat regulators as adversaries, but partners in ensuring safe and effective treatments reach patients.

"People sometimes view regulators as somewhat of an adversary – they're the gatekeepers," he adds. "You want your gatekeeper to understand what you're doing. You don't want to hide stuff. You don't want to be brief. You want to be as voluble as necessary."

Partnering with regulators also means taking advantage of every available FDA meeting opportunity.

> "The best optimizers may lie in strategic planning and working with experienced thought partners to create the most effective approach."

> Sponsors who invest in thoughtful planning and expert guidance will be best positioned for success.

The Agency typically grants sponsors 5-9 chances to meet with them. Successful companies use these interactions to build relationships and gain valuable guidance.

"If you want a great lesson to learn in drug development," Weinberg said, "take every meeting with FDA you can."

Plan For Device Regulatory Review

Combination products, like biomarker assays, often carry a device portion that will need its own regulatory review. One of the biggest issues Weinberg often encounters is developers not thinking through the device application for these products.

"Nothing about drug development should be an afterthought," he said. "Everything should be a forethought."

Sponsors putting a biomarker assay through development shouldn't wait till the end for the FDA to request the technical specs. Considering device regulatory requirements earlier—say, during toxicology studies—could help sponsors avoid unnecessary delays.

DON'T LET SPEED BE THE ENEMY OF EXCELLENCE

Sponsors face mounting pressure to accelerate programs while navigating an increasingly complex regulatory landscape. The temptation to sprint through development has never been stronger. Even so, "there isn't a regulatory situation in front of us in which thought shouldn't be your first action," Weinberg said.

The solution isn't to slow down, it's to think smarter. Being thoughtful represents the best future-proofing strategy sponsors can deploy in today's uncertain regulatory environment. This means examining the regulatory landscape and clinical data simultaneously, like a lawyer assessing the forest and the trees before making a critical argument.

His prescription for success is simple: "Be thoughtful and engage people who can help you think." Getting expert help early enables sponsors to structure activities in parallel, generating valuable data sooner while maintaining regulatory rigor. A skilled project manager can bridge the tension between investor urgency and scientific thoroughness.

Sponsors who invest in thoughtful planning and expert guidance will be best positioned for success. The companies that emerge won't necessarily be the fastest—they'll be the most strategic.

References

1. Regulatory Affairs Professionals Society. Thousands of FDA staff fired in latest RIF (2025). Thousands of FDA staff fired in latest RIF (raps.org)
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