Regulatory Expertise Eases the Way for Company's First IND Submission

A young biopharmaceutical company developing a pipeline of preclinical cancer immunotherapy treatments was preparing to file its first investigational new drug (IND) application with the Food and Drug Administration (FDA). New to the submission process, the company had underestimated the complexity of the job and found itself facing a tight two-month deadline—with a single individual in charge of multiple competing programs, few processes in place, and a lack of on-site regulatory experts.

The company hired Integrated Project Management Company, Inc. (IPM) to provide expertise on mitigating quality and regulatory issues, develop best practices for early-stage preclinical drug development, and shepherd the company's first IND submission to completion.

FROM TIMELINE TO DEADLINE

Working closely with the company's senior director of program and alliance management and the IND project team, IPM developed a regulatory submissions structure to get the project on track. Part of the process included creating an integrated product development plan, which included timelines for chemistry, manufacturing, and controls (CMC) activities with contract manufacturing organizations (CMOs), nonclinical studies, meetings with the FDA, IND submission activities, and clinical development actions.

IPM also acted as a liaison between the company and multiple third-party contract research organizations (CROs), which were responsible for coordinating and submitting the IND documentation. IPM led document review and tracking to ensure that all paperwork was in the proper format for FDA submission. This was especially challenging because of the many different document versions that required review by key personnel.

Although the team had an aggressive deadline, everyone collaborated, and the company submitted its first IND to the FDA five days ahead of schedule.

A BUMP IN THE ROAD

However, this was just the beginning of IPM's engagement with the company. A few weeks later, the FDA notified the company that the submission was on clinical hold due to exclusion criteria involving unclear language in the protocol.

To remove the clinical hold and proceed with the IND review, the team had to quickly compile sufficient documentation and meet with the FDA to confirm requirements and answer questions. During that time, the IPM consultant worked side by side with the company's new full-time project manager, mentoring her on the intricacies of regulatory submissions. The FDA removed the clinical hold a month later.

LESSONS LEARNED FROM THE SECOND SUBMISSION

Meanwhile, the company was launching a second IND within another three- to four-month submission timeframe. This project was more complicated than the first: while typical INDs involve one drug substance and one drug product, the second submission involved three drug substances, greatly increasing the amount of documentation required for submission.

IPM partnered with the company project manager to lead the submission effort. IPM also worked with two CMOs and helped build and manage multiple subteams for the submission. Things quickly became complicated for the company project manager, who was coordinating with the clinical team, senior management, and regulatory consultants. The IPM consultant and the project manager found a way to match complementary skill sets and forged a strong partnership. IPM also provided expert Microsoft Project training to strengthen the quality of the interdependencies in the integrated project plans—from discovery, manufacturing, through IND submission, and into the clinic.

A major contribution to the submission's success was IPM's development of an interactive tool that outlined how each piece of information fit into the submission process and graphically displayed how a single delay in one area would affect the whole submission. This tool proved to be so useful that the project sponsor presented it to the entire company as an educational tool on the IND process.

The second IND was not without its challenges. With less than 12 hours remaining before the submission deadline, the IPM consultant used her regulatory experience to identify a critical error in one of the clinical documents—something that had slipped through previous QC/QA reviews.

Once all the documentation was completed, the company successfully submitted the second IND close to the target date, and because of lessons learned from the first submission, there was no clinical hold.

Today, with two successful INDs under its belt, the company is armed with the processes and experience that will help it succeed with future submissions.