



CASE STUDY

Rigorous Coordination Secures On-Time Biopharmaceutical NDA Submission and Launch, Delivering Additional \$12 Million to Bottom Line

PROJECT BACKGROUND

A major pharmaceutical company in-licensed a developmental pharmaceutical product nearing the end of Phase III clinical trials. At the time, the previous owner and a third party manufacturer were deeply engaged with managing the complex regulatory filing procedures for the new drug, validating an unreliable manufacturing process, and understanding the technology deficiencies that were producing too many molecular variants to pass the rigor of agency scrutiny. Many of the new owner's senior managers stated that it might be impossible to turn this project around and obtain FDA approval. The extraordinary effort required, however, was deemed worthwhile because if approved it would be the first biological drug to market for the company and for the particular indication sought. In addition, the drug had high potential for treating other indications, thereby generating a significant revenue stream for the company. The new owner of the product completed due diligence to identify the breadth of the issues associated with the project, which included some major obstacles that

seriously jeopardized the probability of success.

IPM'S SOLUTION

The company realized that the project risks could only be minimized through the disciplined application of project management including implementation of an effective team and communication structure, rigorously planning, and effective leadership to drive collaboration between the many stakeholders. Consequently, the company retained Integrated Project Management Company, Inc. (IPM) to provide professional project management services to the existing eight functional teams focused to achieving licensure as rapidly as possible. The project's stakeholders included engineers, managers, and scientists from the functional disciplines of analytical, manufacturing management, quality assurance, regulatory, and process technology. Immediately upon deployment to these functional teams, IPM improved and documented the overall project structure and the interdependencies. Within teams, IPM provided acutely needed meeting structure (leadership, facilitation, agendas, minutes, follow-up, and accountability). Project

plans and schedules were developed for each team and linked to an overall plan.

Within six months of IPM deployment an 'approvable' letter was received from the FDA that indicated the new drug could be approved if specific deficiencies were addressed. These deficiencies numbered well over one hundred, most requiring intense efforts to refine the manufacturing process, analytical methods, and product development documentation systems. Gathering the required competencies for strategic planning meetings, IPM facilitated sessions to discuss and plan the approach to respond to and assign responsibilities for resolving each of the issues, including sessions to identify and characterize breakthrough biologic manufacturing process improvements aimed at minimizing the molecular variants in the product. The final strategy session focused on defining a mutually agreeable timeline, with the group concluding that an aggressive 12-month schedule would be required to respond completely to the FDA's concerns and assure sufficient product supply and logistics

coordination to support launch within 48 hours of approval. An adjunct risk management plan was also created to minimize the impact of project uncertainties inherent in the technology development and regulatory approval processes.

The teams encountered many of the predicted obstacles as they progressed through the project plan and schedule. All these issues were resolved by the perseverance and flexibility of the teams led by the focused IPM project managers. One such technology related obstacle included a new requirement from the FDA that extended the duration of a key product quality test (stability) from three months to six months and required submission of the data to the FDA for review prior to its approval of the product. Working with the functional area leadership team to identify opportunities to compress the schedule, IPM extracted non-traditional ideas from the participants to accommodate the FDA's request, while maintaining the original 12-month schedule for submitting the revised New Drug Application (NDA).

The team also encountered a complex regulatory filing due to schedule constraints and the global transition to the Common Technical Document (CTD) format adopted by the International Conference on Harmonization (ICH). The company needed to accurately convert the existing NDA and MAA submission documentation into the CTD format within the 12-month project timeline. IPM managed the conversion process for the on-time submission as well as

subsequent filings in Canada, Europe, Japan, and the rest of world (ROW). IPM accomplished this challenging objective by developing an overall, worldwide Regulatory Submission Project Plan and Schedule to ensure alignment of both the project submission schedules and the CTD conversion activities. IPM also developed a strategy and work process to efficiently utilize the client's pilot CTD document management system to map and convert the existing submission format into the new CTD format. Additionally, IPM developed a tracking tool to identify and confirm the technical accuracy and status of all submission components completed by the functional resources.

PROJECT RESULTS

The NDA was submitted and approved by the FDA without delay, and the product was launched within 48 hours following approval.

Throughout the course of the project, a variety of unforeseen obstacles threatened to delay the submission by a cumulative seven months. The ability to avoid these potential delays, which represents over 50% of the 12 month baseline schedule, was attributed to the disciplined and rigorous approach to planning, scenario analysis, and risk mitigation, as well as seamless communication and effective facilitation provided by IPM's professional project managers working in collaboration with the functional area experts. The incremental profit associated with this time savings has a calculated NPV of \$9.2 MM. On time or ahead

of schedule completion of technology development and submission-related activities and better than anticipated production yields realized a cost savings of \$3.1 MM.



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