

Success Factors for NDA/BLA Preparation



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How should you plan for an NDA or BLA?

The process by which the NDA/BLA is prepared, submitted, and supported throughout its evaluation is a key component of the timely approval and launch of a new drug or biologic product. Numerous important process issues and considerations must be addressed to maximize success, starting with early planning.

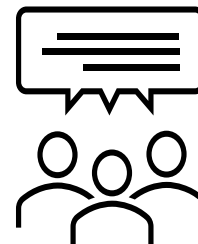
Planning begins with a clear understanding of the goals and objectives of the project. An important next step is to form an appropriately qualified cross-functional team from which to obtain expert input (as well as management's) on the plan. The plan should incorporate the appropriate research and development elements and follow the latest regulatory requirements and guidelines. It should be reviewed and updated periodically to reflect changes in the environment, both internal (i.e., chemistry, pre-clinical and clinical data) and external (e.g., competitive landscape, regulatory requirements, standards of clinical care, etc.).

How do you execute your NDA / BLA plan?

Once the plan is in place and the line units are all working to gather data, the next step is to lay the groundwork for the preparation of the NDA or BLA. This includes developing internal standards for data handling, document preparation and control, and quality assurance procedures consistent with regulatory requirements and guidelines. Line units should all become familiar with required document standards (eCTD modules, headings, TOC hierarchy). A useful tool to guide the preparation of the application is a draft NDA/BLA index, addressing all required components (FDA forms, required summaries/tabulations, etc.) and listing each of the anticipated internal line unit reports. Like the overall plan, the draft index should be reviewed and updated periodically.

As the last of the studies (typically the pivotal efficacy study) nears completion, it is time to initiate NDA/BLA submission activities, including but not limited to

- i. Confirm that all NDA/BLA components are available electronically and in a format which is acceptable to the health authorities.
- ii. Know what, where, and how to submit via FDA's portal;
- iii. Plan for the pre-NDA/BLA meeting with FDA and schedule it in time to incorporate agency feedback. Make all line units aware of this opportunity to seek agreement/guidance from FDA on anticipated content and format issues.



The next step is to plan for activities to support FDA's review, approval, and launch. This includes ensuring that each line function remains ready to respond promptly to FDA inquiries during the review. This need is highest and most intense during the three or so months prior to

the action date. Fast turn-around time is essential to a timely approval. In addition, it's also critical to anticipate the need for a revised draft, annotated, and final labeling, and alert the CMC and clinical line units to be ready to support upcoming FDA pre-approval site inspections.

Moreover, planning is also necessary for post-approval and launch activities. FDA approval letters typically include several mandatory commitments, including safety update reporting, submission of launch advertising for pre-clearance, submission of updated stability data and/or physical samples, post-marketing studies (special populations, i.e., pediatrics) etc. Also, the time between approval and launch is when launch supplies are prepared, marketing materials are developed, and sales representative training takes place. Members of the project team should be available if called on to support these time-sensitive activities.

What are the less tangible factors that contribute to a successful NDA/BLA success?

- First among them is knowledgeable, competent, and consistent leadership of the entire process. The process is long and quite complex, and there will be challenges along the way. A leader who is dedicated, with a broad understanding and knowledge of drug development and is skillful in managing people and overcoming challenges, is essential to success.
- Effective communication, among project team members and between the project team and management, is another important factor for success. Team members must be encouraged to solve problems with the help of other team members without having to go to the team leader first. When issues, both small and large, are allowed to come to the surface in a timely manner, delays can be avoided and, if necessary, plans can be adjusted with minimal impact.
- Organizational and team commitment is another less quantifiable asset. Preparing an NDA is a very large and complex task involving many process steps, interdependencies, analyses, checkpoints, endpoints, and handoffs. In addition, unanticipated results and factors beyond the team's control (slow enrollment, delays at the contractor level, etc.) may challenge the process. Commitment, both from senior management and among the team, to address these challenges (by allotting additional resources or by working late, for example) becomes a success factor when this happens.
- Finally, since the goal of the process is to achieve regulatory (FDA) approval, each team member must help share the role of drug regulatory affairs (DRA). This means that everyone should make an effort to become familiar with all the regulatory requirements associated with their work and see that they are followed. Likewise, DRA should have an open-door policy when team members need to seek regulatory advice.