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Successful Regulatory Submission

Via the Trifecta of Awesomeness

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The regulatory submission process is inherently complex, regularly presenting submission teams with a broad set of challenges, both common and unique. Factors ranging from inexperienced team members and rushed timelines to a lack of internal alignment on messaging can undermine submission quality and slow the process to a crawl. However, three essential elements contribute to a repeatable, adaptable submission process. This “trifecta of awesomeness” includes strategic planning, team engagement, and properly leveraging team experience.

Strategic Planning Builds the Foundation for Successful Submission

Imagine you are building a house. The need for shelter is urgent and build quality is important, lest the structure collapse during its first storm. Will both speed and quality be served by starting to pour concrete and erect framing immediately? Or is it better to first pause and consider what is being built, how, and by whom? Using a physical example, the answer seems obvious, but these principles can be more easily forgotten with something more abstract, like a new drug application (NDA).

It is common for contract research organizations (CROs) to assume that, because they have completed numerous regulatory submissions, they know what a “good” one looks like and can jump in right away. Once draft one is complete, the customer can review for what to add, cut, or adjust. But that strategy is equivalent to a contractor building a home before asking its customer for any design specifications and then spending time and resources redesigning, tearing things down, and reconstructing.

Strategically planning medical writing means fewer rewrites, higher document quality, and greater likelihood of a successful submission — versus delays, lower document quality, rework, and a frustrated team. Four key factors contribute to effective strategic planning: foundational documents, document blueprints, calculated timelines, and early input from senior leadership.

1. Foundational Documents

Before building anything, logic dictates the establishment of common, consistent core building materials. For submissions, these are foundational documents that should be established before a single submission document is written. They include a style guide as well as a lexicon or harmonized terms, so all writers are using the same words in the same way. Foundational documents also comprise common background text about the disease and the drug, information that could confuse regulatory reviewers if written differently across different documents.

Perhaps most important is the submission’s key messages document, which captures information like product risks and benefits. Essentially, it serves as your elevator pitch to regulatory reviewers and provides a great opportunity to proactively address any issues you anticipate with your submission. If you can establish those foundational pieces up front, before building other documents, the submission will provide a more logical presentation of information for both internal and regulatory reviewers.

2. Document Blueprints

Another factor in strategic planning is early input from team members. The team should work together to develop a plan, or blueprint, for the document before writing begins. One strategy is to develop a robust pre-data draft of the methodology containing mocked-up results that includes as much detail as possible. Another is storyboarding a document shell, using placeholder text with a table of contents, so it can be determined through meetings with subject matter experts (SMEs) which information is best discussed in text and to what extent.

Starting at the kickoff meeting, remind the team of each review’s specific purpose. Asking for a sample document is always helpful before writing begins because it can help to promote consistency in layout, level of detail, and document tone. As tables, listings, and figures (TLF) shells become available, those deliverables can be reviewed to ensure all required analyses are accounted for and presented in a format appropriate/usable for the document.

Finally, data review meetings are imperative. These provide the submission team an opportunity to discuss the study results and to determine, together, the messaging for each key point before writing begins. Poring over these details at this stage is critical to identifying red flags before they evolve into more tangible, costly problems. It can take a lot of time and resources to obtain important missing TLFs, correct unusable TLFs, or rewrite a document missing key messages after the fact, versus pre-planning and making sure everything is in place before writing begins.

3. Calculated Timelines

The timeline element of strategic planning comprises thinking about how all the pieces of a submission fit together. For example, a medical writing team needs to engage numerous specialists and must consider the availability of those individuals and teams as well as how they will work together. To plot timelines with maximum effectiveness and efficiency:

- Develop timelines with resource availability in mind, planning around the availability of SMEs and other important stakeholders for each topic.

- Plan for thoughtful reuse of text (e.g., background information, clinical program details) and the proper flow of information (e.g., from the clinical study reports to the summary documents).

- Stabilize predecessor content before writing the dependent text. This step prevents the need to return to source documents to discover changes made since the last update. It also ensures the team doesn't inadvertently develop the same content in contradictory ways in different documents.

- Evaluate and reevaluate the critical path. Determine which documents have more flexible timelines and can be adjusted versus those that are more rigid. As things change during the writing process, the critical path may need to be revisited.

4. Early Input from Senior Leadership

Strategic planning for final approval includes gathering senior leadership input early in the writing process. Every detail does not need to be reviewed, but leadership's understanding and approval regarding key decisions, such as main points in the key messages document, should be clear. Data surprises can create issues with messages or presentation. Writers generally know what to expect from TLFs, but when unexpected twists arise, it is vital to hit pause as a team, talk about how you're going to handle it, and run that decision by senior management.

Team Engagement Builds Trust and Capability

Team engagement hinges on shared values, clear expectations, and fluid communication. A high-functioning team starts with trust. Each member can count on colleagues to show up every day committed to working well independently toward their shared purpose, which minimizes or eliminates hovering and micromanagement. Like any other capability, submission team cohesiveness requires an investment of time and effort — relationship-building to foster and reinforce shared values and attributes surrounding collaboration, decisiveness, personal accountability, mutual respect, and reliability.

Regarding expectation setting, the "project management triangle" (Fig. 1) provides an apt visualization of the constraints on any project that make it impossible to file quickly, using minimal resources, and still produce the highest-quality product. Success requires prioritization and resourcefulness around these elements. Producing high-quality documents on a fast timeline is resource intensive, taking ample time and money, but more importantly, strategic planning, pre-work, building a cohesive team, leveling up on technology and processes, and making sure the team has the bandwidth to focus are keys to achieving success.

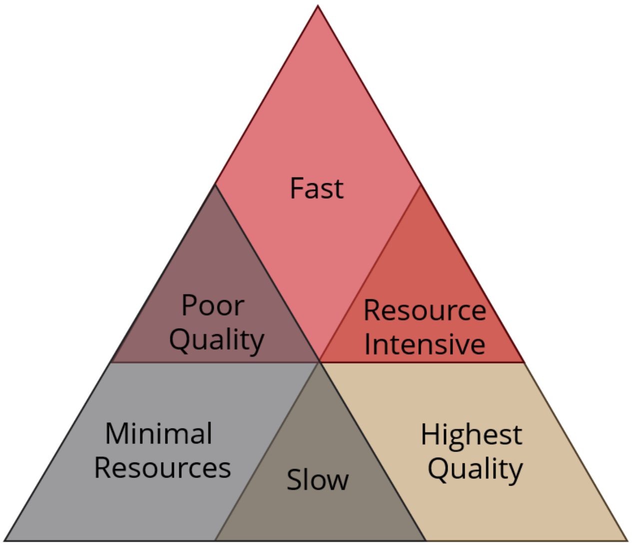

Fig. 1: Setting expectations via the "project management triangle"

The third key aspect of team engagement is communication, and its most basic principle is perspective taking – placing yourself in the other person's shoes. Respect the message recipient's time and energy by ensuring every interaction communicates something of value. Notably, many tasks completed via a meeting or a phone call can later be sent as a teamwide email to provide confirmation and to promote team awareness. Additionally:

- Keep it simple! Keep missives brief and to the point. If you can't pose a question or present an explanation simply, a team or one-on-one meeting may be necessary.
- Practice meeting etiquette: Send an agenda and stick to it, send pre-reads, and end on time.
- Use consistent messaging. Do not be afraid to present the same slides more than once, and share out-of-office (OOO) time and review scheduling in a team calendar.
- Establish explicit lines of communication so the team isn't wading through emails for answers and to prevent contradictory feedback between writers or across documents.
- Establish daily standup meetings. Don't sit down and get comfortable: stand there for 15 minutes, talk through the business of the day, and get back to work.

Experience is the Sum of its Parts

Time in industry and the number of submissions a team or individual has handled are broadly recognized as indicative of submission experience. They imply knowledge about success strategies, organization, and pitfalls. But experience is only as valid as the organized practices or skills it begets, such as:

- **Exposure —** Has the person heard about or directly experienced a particular scenario before?
- **Participation —** Has the person actually written the documents in question? How many times?
- **Leadership —** How often a team member has accomplished a task is important because repetition builds familiarity, which aids them in directing others regarding what actions must be taken and when.

- **Prediction —** Depth of experience contributes to a writer's ability to envision challenges to come in the process.

- **Troubleshooting —** Being able to foresee some issues, understanding their root causes, and having knowledge of previous effective solutions all contribute to a writer's ability to troubleshoot and fix problems as they come up. More importantly, such writers can devise proactive solutions and contingency plans, which circles back to strategic planning.

If experience is lacking on a submission team, a number of remedies exist to address the issue (Fig. 2):

Leadership	Knowledge	Cohesion	Calm
• Lead where/ when you can • Empower others to step up	• Educate/ mentor • Increase visibility and participation	• Facilitate communication • Foster connections • Direct inquiries	• Show progress • Contingency plans • Contain the panic

Fig. 2: Potential solutions to address inexperience on a submission team

Notably, it is valuable to have different "flavors" of experience on a team, as well as the ability to meld them together into a recipe for success. Some team members may have clinical or scientific knowledge about the disease state or condition. Others have overcome a variety of regulatory hurdles and understand well what the agency wants to see. These team members provide a vital support system to newer or inexperienced team members.

One of the most overlooked boons of experience is adaptability. Experience in being creative and coming up with new solutions when things did not go as planned in a previous submission is invaluable. For example, flexible thought is required to read regulatory requirements that were not written with gene therapy in mind (e.g., pharmacokinetics or drug-drug interactions) or to include information on integration site analysis, for which no space on the document templates may exist.

Embrace the Trifecta of Awesomeness

The regulatory submission process rarely goes smoothly. Thus, it is vital that submission teams be well-prepared, organized, and capable of handling any obstacles in their path. This combination of attributes starts with strategic planning built on the pillars outlined above: submission-wide foundational documents; agreed-upon document blueprints that guide writing; timelines planned with resource availability and critical path in mind; and senior management input, sought early and often.

Adept medical writing also depends on team engagement. Take the time to build relationships, and practice adopting the other person's perspective. Finally, experience is helpful only if team members' expertise is applied thoughtfully and solutions are proactively identified and applied to help guide less-experienced team members. To learn more, visit https://inseptiongroup.com.

About inSeption Group

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