Article | Regulatory Strategy

Chapter 6

A clear regulatory strategy: Maximizing development productivity by keeping the end in mind

Executive Summary:

Every drug or product development journey should begin with the end goals in mind. Early development of a regulatory strategy, as it relates to critical planning data/documents, allows drug sponsors to streamline clinical trials and prepare for regulatory submissions, ensuring optimal outcomes. Two specific planning documents—the Target Product Profile (TPP) and Comprehensive or Clinical Development Plan (CDP)—provide critical blueprints that help inform these efforts. However, too often, drug developers underestimate the vital importance of these planning documents or fail to devote sufficient time and resources to developing them early enough in the process. This can create costly consequences related to budget and timeline escalation, pervasive quality issues and other pitfalls, all of which can hinder regulatory approval and delay product launch. This article examines the roles of TPP and CDP documents in aligning drug development efforts with product attributes, regulatory requirements and market needs.

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Drug or product developers (for simplicity herein, we will use the term drug developers) are aware of the importance of regulatory strategy as they are preparing for regulatory submissions at critical points throughout the timeline of any clinical trial. Gaining regulatory approval is a foundational objective because it opens the door to commercialization—but the ability to realize the full value of any new therapy does not happen in a vacuum. It requires detailed consideration of factors that will support the broadest possible market access for the new treatment.

The comprehensive clinical and commercial value of any therapy or drug franchise can only be fully realized if the approved medication is widely prescribed by healthcare providers and covered by most healthcare plans or health authorities. Early planning in clinical development can demonstrate the value of the new therapy, leading to wider coverage and increased use.

Creating a blueprint for success

Due to a wide range of factors, many drug developers do not devote sufficient attention or resources early enough in the process to prepare two critical planning documents: the Target Product Profile (TPP) and the Comprehensive or Clinical Development Plan (CDP). This creates costly implications in terms of both missed opportunities throughout the clinical development program and increased financial exposure for the sponsor. Such risks come in many forms—including timeline and budget escalation throughout the trial, as well as the potential for delayed regulatory approval and product launch.

Many promising therapy options offer opportunities for more than one indication to be pursued during drug development if the sponsor has the required budget and capacity to do so. The ability to critically evaluate and compare all competing options early (by developing detailed TPP and CDP documents discussed here) provides data-driven insights that can help sponsors prioritize the most promising opportunities.

The time and effort spent to craft thoughtful, in-depth TPP and CDP documents early in the drug-development process creates value for drug sponsors. Such value is defined in many ways. These include improved trial efficiency that delivers tangible results, such as shorter development timelines, reduced expenditures, increased overall quality, and improved patient and trial investigator experiences. Meanwhile, value in drug development also comes from the long-term impact the new therapy has for patients and providers, helping to improve clinical outcomes, reduce healthcare expenditures and more. For example, early planning efforts (guided by the development of robust TPP and CDP documents) may help sponsors to identify opportunities for product differentiation, such as improved dosing intervals and other methods of drug administration, that could help to improve patient adherence to therapy and thus improve outcomes.

Such due diligence can help the sponsor to identify which indication(s):

- Have the potential to be the most successful from an overall market-value perspective
- Could meet critical unmet medical needs among patients
- Could help the sponsor support or extend an existing drug portfolio or franchise

The TPP and CDP documents, when created early in the drug development process, provide the sponsor and its chosen contract research organization (CRO) collaborators with a data-driven rationale to characterize the clinical and commercial value proposition of the promising new therapy. Such insights can inform trial activities and help the drug sponsor articulate relevant details more effectively during regulatory submission efforts. A robust regulatory strategy serves as the foundation for navigating the complex and evolving landscape of global pharmaceutical regulations, ensuring that new therapies reach patients efficiently and safely. Meanwhile, overall trial productivity can be improved by minimizing protocol amendments and avoiding surprises that could create delays—or worse, lead to costly, late-stage failures when seeking regulatory approval.*

The TPP and CDP documents also provide detailed support of specific regulatory requirements when the investigational therapy is being pursued to address an unmet medical need and the sponsor is considering pursuing expedited pathways—including accelerated approval, or is planning to seek potential expedited program provisions that may be available based on the specific therapy (for instance, orphan drug designation for specific cases where the investigational therapy addresses a rare disease, or fast track, breakthrough therapy, PRIME or Sakigake designation for a product that treats an unmet medical need). This underscores the importance of expending time and effort as early as possible in the process to develop thoughtful and complete TPP and CDP documents.

The impact of poor preparation is a pervasive issue across the drug development landscape. According to one industry estimate, between 2000 and 2012, 47% of new molecular entities (NMEs) submitted for FDA approval were delayed due to scientific and regulatory reasons.[1]

Similarly, a recent study by the Tufts Center for the Study of Drug Development[2] found that the mean number of trial protocol amendments increased from 2.1 to 3.3 between 2015 and 2022, creating costly budget and timeline impacts.

As noted, the TPP and the CDP[3] play a crucial role in informing clinical trial development and execution, which can improve the odds of success during regulatory submissions and market access planning. Each is discussed in greater detail below.

Target Product Profile—The TPP outlines the anticipated characteristics of the new drug product and establishes such critical attributes as:

- Potential indication(s) and usage
- Dosage and administration
- Safety
- Efficacy
- Contraindications
- Adverse reactions and drug interactions
- Additional proposed label language and more

The TPP also seeks to differentiate the investigational therapy from existing therapy options in the same therapeutic niche, which helps drug developers to better understand the potential value of the new product in relation to competitor products and unmet medical need.

Meanwhile, efforts to establish what clinical and commercial role the final product may play within the healthcare landscape (in terms of clinical indication(s), patient population and more) early in the drug development process inform trial design and execution and helps the sponsor to identify and address evidence gaps early in the process. This can help to inform the proposed label language and streamline and strengthen the regulatory submission process.

While the development of the TPP is voluntary, regulators encourage drug developers to produce and submit this detailed planning document to guide the clinical development process and create a roadmap that fully envisions the final intended product. Such effort facilitates discussions with regulatory decision-makers.

Clinical Development Plan—The CDP provides additional details (based on findings developed in the TPP) to inform clinical development and market access strategies. In particular, the CDP aims to anticipate the specific requirements

* This paper is part of a multi-part thought leadership series on how to improve productivity throughout all stages of the clinical trial. All chapters can be found at **www.fortrea.com/insights**

necessary to achieve regulatory approval, so the clinical trial is designed to yield the required insights. The goal is to anticipate the information needs— and not wait for evidence gaps to emerge later in the process.

The CDP typically includes specific information related to budget estimates, personnel assignments and timelines. Such details are crucial for coordinating clinical activities, such as the sequence of specific studies, specific objectives, endpoints and more. Importantly, the CDP also establishes critical "Go/No-Go" criteria the drug sponsor will use to advance or suspend the clinical development of the investigational therapy.

When developing both the TPP and CDP, it is important to integrate input from multi-disciplinary stakeholders and foster collaboration among clinical, regulatory, commercial and other teams. This ensures that all parties share a common vision for the new therapy and the process for bringing the new therapy to market. Formalizing such details in these central planning documents ensures that all stakeholders are aligned on timelines and important milestones.

As with the TPP, the CDP is also a voluntary document. It is important to remember that both documents are not final once they are developed. Rather, both are dynamic documents that should continue to evolve as additional data-driven insights, changing market dynamics and other drivers become available.

Different drug sponsors face different challenges

Individual drug developers vary in terms of whether they possess sufficient internal expertise, experience and access to the necessary resources required to develop the TPP and CDP documents. Drug developers, both large and small, can benefit from working with a third-party CRO that has explicit drug/product development consulting expertise and experience developing and refining TPPs and CDPs to optimize market access. Such a partnership can help the innovator company to prepare these important planning documents in ways that optimize both the clinical trial and the regulatory strategy (For more discussion on the value of working with a CRO with product development consulting expertise, see the Sidebar Box on page five).

Larger, established pharma companies

As noted above, larger drug developers are often able to pursue multiple potential indications for a given investigational therapy. Such parallel options help them to capitalize on promising market opportunities, address unmet clinical needs or augment an existing drug portfolio or franchise.

When sponsors devote the time and resources needed to develop the TPP and CDP documents early in the process, they can better articulate and evaluate parallel opportunities associated with the promising new therapy. Formalized planning documents help the drug developer to identify opportunities that may offer significant clinical and commercial benefits for the company and the healthcare community, as well as recognizing which indications may involve higher levels of risk.

Larger established pharma companies often have a broad base of internal experience and expertise when it comes to creating thoughtful, detailed TPP and CDP documents. Collaborating with a CRO that has product development consulting experience (and specific experience and expertise to support robust TPP and CDP development) can bring a fresh perspective (to break from familiar patterns of operation and the status quo) and it can help to challenge the status quo and encourage greater cross-departmental collaboration.

Emerging biotech companies

By contrast, emerging biotech companies are typically resource-constrained in terms of internal personnel, clinical and commercial expertise and budget availability. Such emerging companies may not recognize the critical importance of these planning documents and may not have the budget or bandwidth to create them on their own.

Without a detailed planning framework, emerging drug developers may miss chances to develop drugs rationally and efficiently. And they may miss the opportunity to develop critical insights and criteria to inform the "Go/No-Go" strategy for therapy.

Meanwhile, due to prevailing resource constraints, emerging drug developers often cannot pursue multiple indications for a promising investigational therapy simultaneously. Creating detailed TPP and CDP documents early in the process can provide a more data-driven basis for deciding which indication will provide the best clinical and commercial opportunity for the company and the healthcare community.

Meanwhile, committing the time and resources needed to create a more thoughtful, rational, data-driven approach to clinical development also strengthens the company's position when it comes to planning its exit strategy. Such insights help the drug developer to articulate the full value proposition of the clinical asset, which is critical for driving the most valuable merger, acquisition or licensing opportunities. Working closely with an experienced CRO can help emerging biopharma companies overcome limitations that may undermine their ability to develop the TPP and CDP documents on their own.

How a CRO partner with product development expertise can help prepare your regulatory strategy and streamline trial execution

Working with an experienced CRO, drug or product developers of any size gain access to a knowledgeable and experienced collaborator that can help them manage drug or product development complexities and avoid pitfalls and productivity drag in the most strategic way. Experienced CROs bring broad and deep expertise to the table—but not every CRO is explicitly skilled in TPP and CDP development and has vast experience across different types of therapy, therapeutic indications and geographic spaces.

CROs with product development expertise are also able to help drug sponsors recognize broader trends and opportunities that may benefit the drug or product development effort. Such insights can sharpen the focus—or in some cases change the strategic direction—when the investigational therapy has multiple potential indications, patient cohorts or target market sectors. The goal is to ensure that the investigational therapy is positioned to reap the strongest long-term rewards in terms of its clinical and commercial profile and that the clinical trial is operated as productively as possible.

Specifically, CROs with product development expertise are able to provide experience, context, insights and expertise that can help the drug sponsor to:

- Support all types of regulatory agency interactions
- Provide scientific reviews and gap analysis to strengthen the available data
- Prepare documents in the form that is most appropriate
- Support specific regulatory requirements related to the pursuit of expedited pathways (including accelerated approval, orphan drug designation and more), where appropriate
- Support planning beyond the initial regulatory approval (i.e., reimbursement strategy, payer insights, value proposition development, health economic modeling, etc.)

Closing thoughts

Any purposeful journey should begin with a clear destination in mind. Mapping that journey is essential to get there expediently. But arriving at that destination only to realize that you have left something important back at the start means at minimum a missed opportunity, or at worse, going back to get what is missing. Starting the process by envisioning the end goals helps stakeholders to be really clear about the destination, about the route needed to get there and about what must be done along the way.

Demonstrating the therapeutic efficacy and safety of an investigational therapy is mandatory during drug or product development. However, these benchmarks alone are insufficient to ensure the most productive clinical trial, and do not guarantee a satisfactory regulatory review, a successful product launch or effective commercialization. Efforts to lay the groundwork for these equally important objectives begin long before the clinical trial gets underway. Toward that end, drug or product developers can drive efficiency and improve their chance of success when they articulate their end goals early in the process and use them to inform the drug- or product development process.

A company's willingness to invest the time and effort to develop the detailed TPP and CDP documents discussed here is critical to setting the new therapy up for success. Sponsors that prioritize the development of such a data-driven planning framework are in a much better position to both improve productivity throughout the clinical trial (by reducing avoidable timeline and budget escalation, reducing quality issues and risk) and develop evidence-based regulatory packages absent critical gaps in data.

While efforts to develop TPP and CDP documents require time and money, the potential return on this investment delivers benefits in a number of ways:

- Anticipating and developing the information and data needed to position the product for regulatory success, differentiate the product, identify critical "Go/No-Go" criteria to know when to stop, and in doing so, to improve the likelihood of regulatory approval
- Evaluating major clinical development issues/risks (based on experience and lessons learned) to avoid pitfalls in new development programs
- Positioning the new therapy for broader adoption by, physicians and payers, and stronger long-term performance against competitor therapies in the same therapeutic space through the targeted development of key evidence

If developers don't have the expertise or resources internally, the right CRO can be a great thought partner for planning or execution of the regulatory strategy. You don't have to do it alone.

References

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Alicia Baker McDowell is Head of Regulatory Strategy and Product Development Consulting at Fortrea. Alicia has more than 29 years of drug development experience, 26 years of which have been spent in global regulatory strategy. Alicia has registered products in more than 90 countries worldwide and is experienced in direct agency interactions with health authorities, including the U.S. Food and Drug Administration (US FDA), European Medicines Agency (EMA), Health Canada – Health Products and Food Branch (HPFB-HC), U.K.'s Medicines and Healthcare Products Regulatory Agency (MHRA), China's National Medical Products Administration (NMPA), Japan's Pharmaceutical and Medical Devices Agency (PMDA), South Korea's Ministry of Food and Drug Safety (KFDA; formerly known as Korea Food and Drug Administration), Australia's Therapeutic Goods Administration (TGA) and others. Her experience spans small molecules, biologics, advanced therapies, diagnostics and medical devices across multiple therapeutic areas. She is well-versed in rare disease development, and expedited development pathways and designations. She led the development of Clinical Trial Diversity Plans at Fortrea, transitioning it into a strategic offering for clients, with the team engaged in writing more than 50 Diversity Action Plans to date.

Alicia leads a team of seasoned product development directors, regulatory strategists who are experts in nonclinical, clinical and chemistry, manufacturing and controls (CMC) development, regulatory writers, publishing and submissions. Her team manages 40-50 agency meetings per year around the globe.

Alicia has a BS in Biology from St. Joseph's University, an MS in Regulatory Affairs/Quality Assurance from Temple University, an MS in Regulatory Science from the University of Southern California, an Executive MBA from Quantic School of Business and Technology and a Doctorate in Regulatory Science from the University of Southern California.

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Teresa Oblak is a clinical regulatory strategist at Fortrea and provides guidance into global development programs across drug classes and therapeutic areas, aiding in the achievement of key regulatory and commercial milestones for sponsors.

Teresa has more than 15 years of drug development experience—the majority within a CRO environment—spanning regulatory affairs, medical writing and value demonstration. Specific to regulatory affairs, she has supported global engagements encompassing deliverables such as clinical regulatory strategy plans, agency meetings and related supportive documents, U.S. IND development and addressing non-hold/clinical hold comments, expedited program applications (e.g., orphan drug designations, fast track designations), special protocol assessments, pediatric plans and diversity action plans. Teresa has facilitated meetings with EMA as well as FDA (CDER and CBER) among a variety of therapeutic areas, including rare and orphan diseases, for small molecules, biologics, biosimilars and combination products.

Before joining Fortrea (formerly Labcorp and Covance), Teresa served as a scientific director and lead writer for a medical communications agency, tackling publication planning and execution for late-stage clinical development programs.

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