



The Critical Path Conundrum

A White Paper Presented by:
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THE CRITICAL PATH CONUNDRUM

I. Introduction

Webster's dictionary defines a conundrum as "a question or problem having only a conjectural answer; an intricate or difficult problem; a mystery". American Heritage Dictionary asserts that a conundrum is "a paradoxical, insoluble, or difficult problem; a dilemma". We all encounter conundrums as we interact with the world, whether in trying to raise our children or manage our careers and lives. It is clear that the biopharmaceutical industry is in the midst of its own conundrum. Both confounding and enabling is the confluence of four key industry catalysts that will help solve the dilemma: evolving standardization, process synchronization, performance optimization and electronic transformation. Every biopharmaceutical endeavor follows a similar pathway or process: research, development, & market (Fig. 1). Contained in this continuum is a critical path of activities (Fig. 2). When considering the critical path, it is easy to derive that quality, cost and speed are paramount in terms of value creation in this gamut.

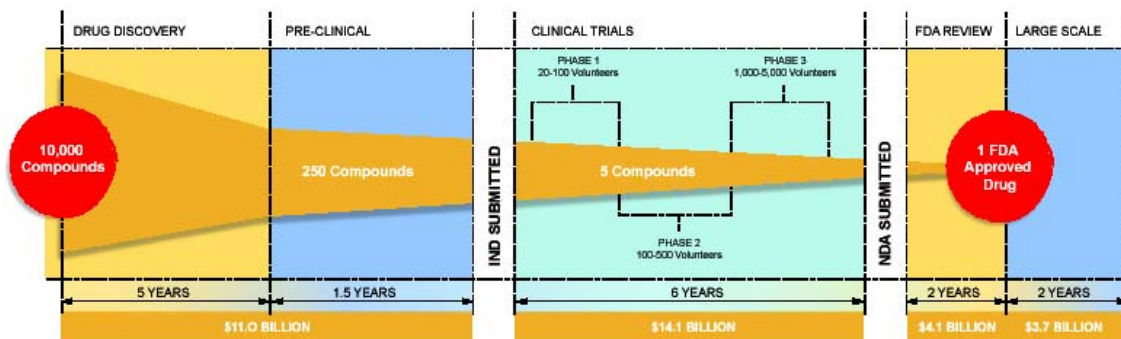


Figure 1. Drug Development. Source: Pharmaceutical Profile 2005, "From Laboratory to Patient: Pathways to Biopharmaceutical Innovation", Pharmaceutical Research and Manufacturers of America, *Pharmaceutical Industry Profile 2005* (Washington, DC: PhRMA, March 2005)

II. Problem Statement

What is the conundrum?

As reported by the Tufts Center for the Study of Drug Development, the costs to bring a new therapy to market are estimated to be between \$0.8 and \$1.7B. There has also been a reported slowdown in new drug and biologic submissions to health authorities worldwide.

As discussed in the March 2004 FDA white paper, *Innovation or Stagnation*, the idealized critical path for the drug development process has born the most recent and staggering cost increases (Fig. 2).



Figure 2. The Critical Path for Clinical Research and Development.
Source: *Innovation or Stagnation: Challenge and Opportunity on the Critical Path to New Medicinal Products*. U.S. Department of Health and Human Services, Food and Drug Administration, March 2004.

The critical path conundrum is that, to date, this system of activities has been addressed with myopic technical and tactical solutions that are task-based and not process-based. Studies of highly complex systems show that, unless a complete understanding of a system exists, a minor attempt to improve one area can lead to disastrous results in the overall system. These issues are certainly not unique to the pharmaceutical industry. Other industries have tackled similar problems but did not have the complexity and regulatory constraints that the pharmaceutical industry possesses. To design a highly integrated, unified system is an extremely complicated effort that introduces intricate levels of complexity into the final process. This complexity can be both difficult to manage and to assess with regard to the impact of change in one area on that in other areas. It is the alignment of processes that is important, aligning the output from one system/department for the input to another and making sure this alignment is producing proper overall deliverables.

Activities at the seams

The goal of seamless integration is often hindered by the critical and chaotic "activity at the seams" (between functions or organizations). This is where we find that process gaps, rework and waste are most likely to occur. Because the process is so complex, traditional solutions focus on picking a task and automating it. Informational roadblocks are a common occurrence in a system that focuses on increasing the efficiency of a particular activity at the task level rather than at the process level. When you create informational roadblocks the larger process slows down, the cost goes up and the overall quality suffers. What has compounded the problem historically is that standards have not been in place to set the stage for process synchronization and other key enablers to change. This is particularly apparent between the functions of Regulatory and Clinical and just as prevalent interdepartmentally within these two larger functions. Of course it is equally relevant to all functional interactions irrespective of departmental size.

III. Solution Statement – A Process Story

An integral part of the solution to the critical path conundrum is that a true capability needs to manifest itself. A capability can be thought of as a set of business processes strategically understood. The key is to connect them to the real needs of the system. Capabilities by definition then transcend functional units and encompass a set of processes interwoven. The aforementioned standards are not the solution per se to the industry's problems. Rather they are a key enabler of the transformation of clinical research and development process

Inherent in the dilemma is the idea that there needs to be change and a reintegration of work. This is predicated on the fact that the organization knows which processes need to be changed, what the processes should be changed to, and how any proposed changes should be evaluated.

Catalysts for Change

There are four catalysts for change enabling the industry to attack the critical path conundrum: Evolving standardization, process synchronization, performance optimization and electronic transformation.

“Standardization” is finally allowing the industry to begin to rethink the way it works. Today, standards are at the forefront of the industry’s efforts to harmonize processes, increase productivity and reduce costs. Standard organizations such as the International Conference on Harmonization (ICH), Health Level 7 (HL7), and Clinical Data Interchange Standards Consortium (CDISC) have given rise to standards such as the eCTD (electronic Common Technical Document), SPL (Structured Product Labeling), & SDTM (Study Data Tabulation Model). These standards have been vital enablers in allowing the industry to begin to revolutionize their process. The electronic common technical document (eCTD) is emerging as an answer for harmonization of the organization of a submission. Although in relative infancy now, it will be the regulatory submission standard on a go-forward basis. The Clinical Data Interchange Standards Consortium (CDISC) has developed a new clinical data interchange standard that is gaining wide acceptance. Specifically, it will support the electronic acquisition, exchange, submission, and archiving of clinical trials data and metadata. In the U.S., Structured Product Labeling (SPL) has been mandated for October, 2005. SPL requires that content of labeling must be submitted electronically. Extensible markup language (XML) is the format for this new label type. The lack of clarity around electronic submissions and clinical data standards should wane as these initiatives evolve.

“Process synchronization” is critical in order to subvert functional isolationism. Another way to state this is that it is human tendency to build barriers between functional areas. Working within these silos instills a prejudiced view of business processes. Technology vendors with a novel technology in search of a process to support are quick to provide ready-out-of-the-box solutions to any problem within a silo. However, this inevitably results in point solutions with dependencies and incompatibilities. Activities at the seams will suffer and become informational roadblocks thus rendering the system dysfunctional.

The “**electronic transformation**” of clinical research and development is a consequence of the need to improve the process of drug development and to speed new therapies to market. A key ingredient to the success of the transformation is the effective implementation of electronic submission methodologies. This transformation is critical to navigate the increasing volume and complexity in submission and clinical development pathways. Technology is a vital component to solving the dilemma. The use of technology enables the user to rethink their process, not just improve or automate it. We can note that processes are only self-correcting to a point. This happens on an informal basis and is manifested in best practices and "work-arounds" that relate to specific tasks. Yet, to realize measurable gains, you have to take it to the next level - redefining processes instead of working around them, integrating tasks and technologies to get greater efficiencies.

Executing tasks and processes is crucial, however, “**performance optimization**” mitigates bottlenecks and rework thus streamlining activities that span the research and development organization. Optimizing processes in real-time will reduce costs, increase productivity and reduce risk.

IV. Enterprise Agility

Processes represent a significant investment, which eventually becomes a corporate asset. They represent the merging of corporate intelligence (understanding how the company works), practical experience (understanding what needs to be done) and technology expertise (understanding how to employ enabling technologies to do it best). Because of this, one can make the point that there is a great deal of intellectual property encompassed in processes. Process visibility and control allow a company to understand and realize the value that may be trapped within the process. Once this process awareness occurs, the company can deliberately exploit the efficiencies and release the value. This builds inherent flexibility into an organization’s strategy by offering the ability to proactively address issues before they impact goals.

Blind Men Touching an Elephant

Information roadblocks created in the process affect cost, time, quality and risk. Operating as a task-focused rather than a process-focused organization creates information roadblocks. Simply creating a more efficient task irrespective of the process will lead to system failure. For a system to succeed, a capability is required (a set of business processes strategically understood). In the clinical R&D arena, how can you consider

eCTD without also considering CDISC? How can you define a regulatory process without also defining and integrating a clinical process? It is important to note that it is critical not to disaggregate capability from technology. Because processes are interwoven between and amongst functions and departments, it is imperative to understand the upstream and downstream deliverable requirements. For example, if you are processing information with limited knowledge regarding the requirements for deliverables, the best case is that existing errors move forward in the process. The worst case is that you add to existing errors. Technology, alone, does not solve this problem. But technology coupled with capability, whether internal or external, does.

The Toyota Way

Toyota revolutionized the automobile manufacturing process. Although a different industry and different finished product, the same basic tenants can be applied to the biopharmaceutical industry. Correlations abound when you consider some of Toyota's guiding principles. For example, "kaizen" or continuous improvement is a central tenant within Toyota. This methodology can and should be applied to the drug development value chain. Too often, work, whether performed internally or via external partners, is processed without optimization in mind. Standardized tasks and processes are the foundation for continuous improvement. Outsourcing is an integral strategy for the pharmaceutical industry yet few outsourcing companies consider continuous improvement in their offerings.

Another Toyota principle that has broad reaching applicability in the biopharmaceutical industry is getting quality right the first time. Traditionally, stove-piped functions have hampered this effort within the drug development supply chain. However as noted above, the four catalysts should enlighten the process to be more collaborative and cross-functional. This is a necessity when considering quality. Cross-functional teams are essential to improve quality and productivity and enhance flow by solving issues.

Process visibility is another important guiding principle that is readily applicable. The use of visual indicators to help people determine immediately whether they are meeting a standard or deviating from it is essential to control the process. You can't repair what you don't know is broken.

V. Summary

True breakthroughs in performance and efficiency only occur when a process approach is employed. As disparate tasks evolve into integrated processes, information barriers dissolve and the strength of the process is revealed. This untapped value can then be exploited throughout the organization in unlimited and recurring settings.

The critical path conundrum needs to be solved. Information silos and stove-piped applications need to be synchronized and harmonized in order to realize time and cost savings. How can Clinical produce an electronic submission-ready deliverable for Regulatory if they don't understand electronic submissions? Conversely, how can Regulatory review output from Clinical if they don't understand something about data standards? Building an eCTD without knowledge of CDISC would be like Toyota building a car and expecting it to run without fuel. It just isn't practical in the changing landscape. Are your functional areas or outsourcing partners equipped to deal with the consequences of informational roadblocks? The emerging standards were contrived to enable a process not a functional area. These standards are converging and usurping historical isolationism. Internal and external partners need to think in terms of a capability rather than in terms of a function or information roadblocks will be created and the process will suffer. In the paper world this caused headaches, in the electronic world it is simply untenable. Think about what would have happened if the automotive industry still employed a silo-based approach? More than likely we would see a new model of car every two to five years instead of every year. The ramifications for the drug industry are much further reaching in terms of getting new drugs and biologics to market. Can we afford to wait a minute more?