

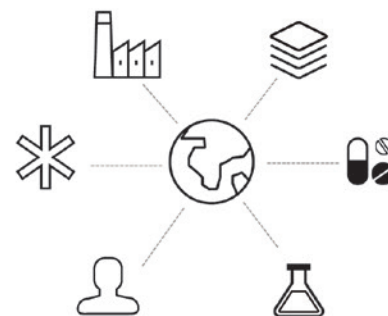
Process PLM: The Future of Pharmaceutical Manufacturing

Introduction

It's been well over a dozen years since *The Wall Street Journal* famously observed that pharmaceutical manufacturing techniques lagged “far behind those of potato-chip and laundry-soap makers.”¹

The same publication made a similarly stark observation more than a decade later, contrasting the “cutting-edge science” driving new drug development with the industry’s long adherence to manufacturing processes “dating to the days of the steam engine.”² On a more positive note, the latter piece described efforts underway to modernize those processes in order to improve quality control and accelerate production.

Indeed, as we will discuss shortly, the industry now appears to be on the precipice of a monumental paradigm shift. Currently, however, the core technologies, concepts and approaches to managing pharmaceutical product knowledge and manufacturing remain dominated by thinking that evolved in the 1980s. Central to that thinking is the regulatory requirement for “documented evidence” that a product is being manufactured according to an approved process. The key word here is “documented.” While the paper-based approach to manufacturing processes that prevailed some 30+ years ago has largely been supplanted by electronic systems, the paradigm is still very much document-based. This, in a world that has been revolutionized by data-driven processes.



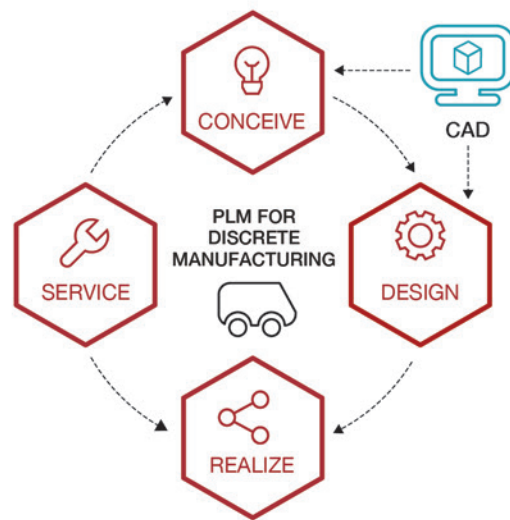
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About the Author

Cathal Strain is CEO of Neo PLM, the company that pioneered digital design-based Process PLM. Cathal founded Neo in 2011 with the vision of bringing third-millennium PLM capabilities to pharmaceutical companies and other process manufacturers. Today, leading pharmaceutical manufacturers are deploying Neo's technology at sites around the world. Cathal previously spent over 30 years at Pfizer, where he led the design, development and implementation of the world's first integrated PLM solution for process manufacturing.

Revolution Takes Root

Ironically, it was that same decade—the 80s—that saw the start of a great metamorphosis in discrete manufacturing. Computer-Aided Design (CAD) technology revolutionized the way goods such as cars and electronics are developed and commercialized by providing a digital definition of the product. That not only unified the management of product knowledge, but allowed the product design to become the central digital structure driving all systems—most notably, through direct interfaces from CAD to Computer-Aided Engineering (CAE) and Computer-Aided Manufacturing (CAM) systems. CAD and 3-D modeling now form the core elements of what is referred to as “Product Lifecycle Management” (“PLM”) in the world of discrete products. There, PLM is a technology-enabled discipline that connects every step in the product lifecycle—enabling radical improvements in product quality and reliability, while dramatically accelerating innovation.



Computer-Aided Design (CAD) is a core PLM application in discrete manufacturing.

In recent years, discrete manufacturers have begun seeking to take that concept of interconnectivity even further with what is being called “Industry 4.0.” The term refers to the idea that a fourth industrial revolution is underway—building on the third, which was the digital revolution. As described by Klaus Schwab of the World Economic Forum, the fourth industrial revolution represents the “shift from simple digitalization... to innovation based on combinations of technologies.”⁴

WHAT IS PLM?

PLM can be broadly defined as a product centric – lifecycle-oriented business model, supported by (information technologies), in which product data are shared among actors, processes and organizations in the different phases of the product lifecycle for achieving desired performances and sustainability for the product and related services.³

– International Journal of Product Lifecycle Management

Current State of Process PLM

That is not to say the concept of PLM is confined to discrete manufacturing. In fact, the topic is being discussed more than ever in the process industries—including pharmaceuticals. Some technology providers even claim to offer PLM capabilities for process manufacturers. The problem there is that drugs and other process-based products cannot be designed using CAD applications—the technology at the very heart of discrete PLM. As a result, so-called PLM solutions for pharmaceutical manufacturing continue to perpetuate the same old paradigm. They are built around a document-centric definition of the end-to-end manufacturing process, and a document-based approach to transferring products from R&D to manufacturing and between plants. Perhaps these solutions—typically, elaborate document management systems with rigorous workflow and change management procedures—can accurately be characterized as “PLM” technologies. However, they simply cannot provide the powerful integration of steps across the product lifecycle that digital product definition enabled in discrete manufacturing. Much of the data required to develop and manufacture new drugs—and even make critical business decisions—remains dispersed among disjointed information systems.



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There are many disadvantages to this fragmented, document-centric approach to managing product knowledge and manufacturing. It is more labor-intensive and error-prone. Accountability and standardization are lacking. Knowledge loss becomes a risk every time the drug-making process moves from one step to another. Perhaps worst of all, after a batch is manufactured, it is impossible to extract execution data in a way that can inform process optimization and business decisions.

However, a confluence of factors is now pushing the industry to finally abandon its old ways in favor of a more modern approach—one destined to increase efficiency, enhance quality and empower innovation much as we just described in discrete manufacturing. As in the discrete world, technology-enabled PLM will again be the key.

Why Has Pharma Lagged Behind?

Before contemplating the transformative change that now appears inevitable, it is worth looking back briefly to understand why pharmaceutical manufacturing has not evolved further to this point. The question may appear particularly puzzling for an industry that continues to make exceptional advancements at the product level. (Like *The Wall Street Journal's* article referencing “the days of the steam engine,” its piece containing the oft-quoted potato chip line noted the irony of companies inventing “futuristic new drugs” while clinging to antiquated processes.¹)

But why the dichotomy? Why do pharmaceutical companies excel at continuously expanding the power of their products to heal, yet lag so many other industries in their approach to managing product knowledge and manufacturing? More specifically, why haven't pharmaceutical manufacturers been able to reap the same benefits from PLM as their counterparts in the discrete world?

We've already touched on a couple reasons, including the fact that many technology vendors actually facilitate today's document-based approaches. Then there is the role of regulatory authorities, which extends beyond their emphasis on “documented evidence.” Under its 2002 initiative entitled “Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach,” the U.S. Food and Drug Administration called for greater advancement in pharmaceutical manufacturing technology. Prior to that, however, the FDA tended to discourage companies from changing their manufacturing processes—or adopting modern technologies.



Digital design tools for process manufacturers have historically been standalone applications that simply cannot integrate with other systems—and enable true PLM—the way CAD does.

Historically, process manufacturers have had no CAD-like application to provide the foundation for a true PLM solution.

While these factors have certainly contributed to the slow emergence of PLM in pharmaceutical manufacturing, there is unquestionably one primary reason. Technology providers to the process industries simply haven't developed solutions capable of addressing the complexity of managing data and information across the product lifecycle in batch-based manufacturing. That brings us back to the lack of a CAD equivalent for this space. Digital design tools for process manufacturers have historically been standalone applications that cannot integrate with other systems—and enable true PLM—the way CAD does.

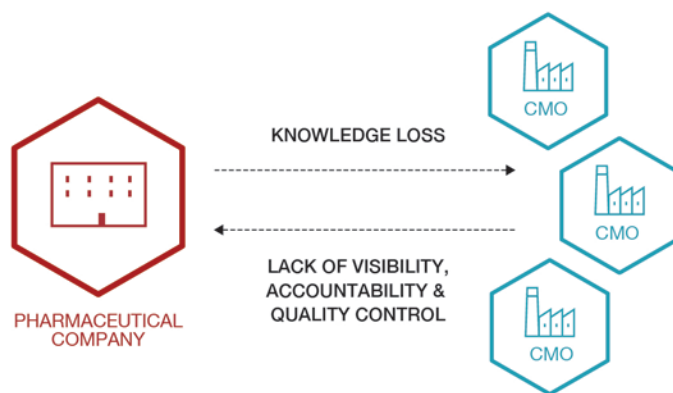
Pressing Need for Change

The fact that PLM for process manufacturing—and the pharmaceutical industry in particular—is being discussed more in recent years represents some measure of progress. However, several trends are now converging to not only push pharmaceutical manufacturing toward a paradigm shift, but make one an urgent necessity.

First is today's globally distributed business environment. As the industry grows increasingly competitive, pharmaceutical companies are recognizing the advantages of partnering with Contract Manufacturing Organizations (CMOs)—and outsourcing production accordingly.

However, while pharmaceutical companies accelerate time to market and reduce production costs through these partnerships, they lose visibility into the critical details of product manufacturing—sacrificing accountability and control over quality management. Then there is the challenge of technical transfers and the risk of knowledge loss. This era of increased outsourcing demands a PLM strategy that integrates pharmaceutical companies with their CMOs—rendering external plants no different from internal departments in terms of information access.

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Without a true Process PLM solution, pharmaceutical companies that partner with CMOs face challenging technical transfers and critical information voids.

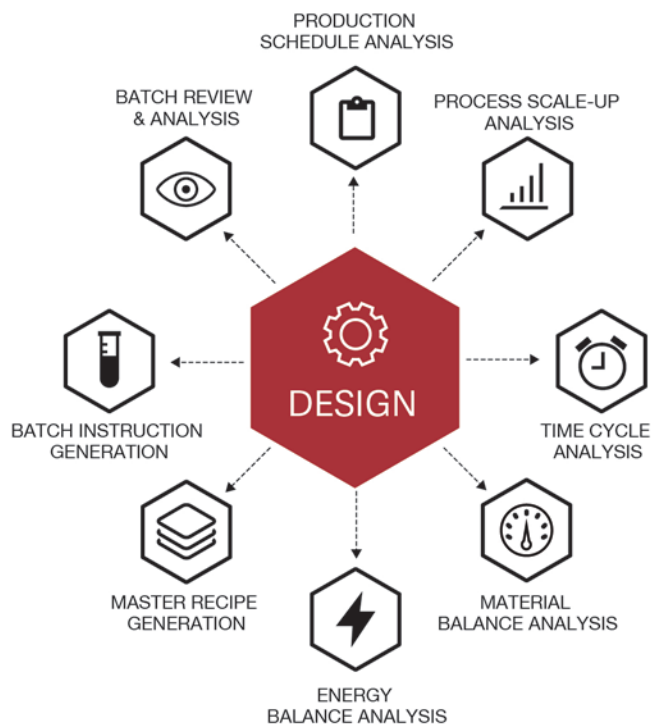
Companies can even have trouble retaining core product knowledge internally in these times of growing employee turnover. Related to this concept, growth by acquisition helps to maintain information silos and—as a result—disjointed approaches to managing process knowledge and manufacturing.

On top of these trends, consider the revolution that has occurred in both consumer and commercial technology over the past 30+ years. Expectations for technology and information access have changed fundamentally. Archaic document-based systems do not meet those expectations, and cannot serve the needs of an industry increasingly populated by personnel raised in the digital age. Technology analogous to discrete PLM is essential to bridging that gap.

The Ideal Solution: Digital Design-Based PLM

By now, the urgency of moving from today's disjointed, document-centric paradigm to an integrated approach enabled by technology-based PLM should be clear. The question then becomes: What exactly does that entail? What would the ideal pharmaceutical PLM solution look like?

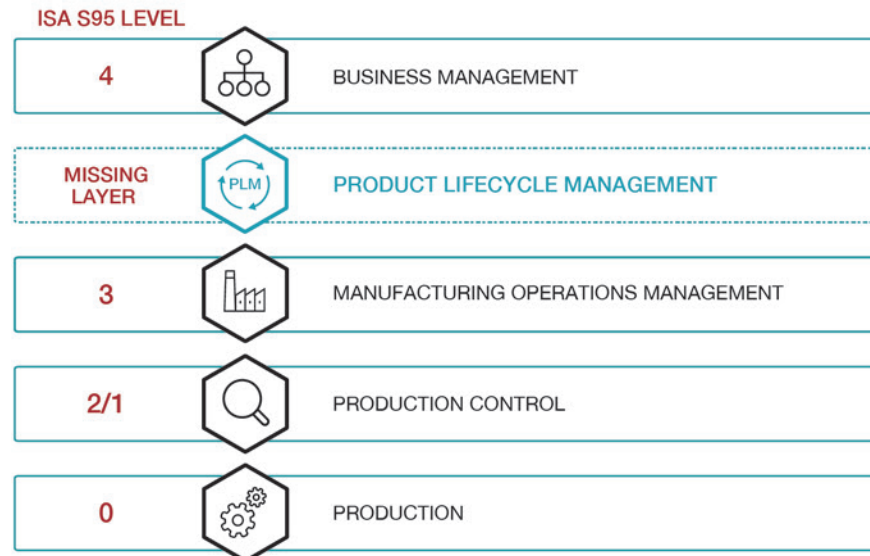
First, as in discrete PLM, the design should be the central structure that drives all systems and connects all stages of the product lifecycle. (We are referring to the product design in the discrete world and its analog in the process industries, the manufacturing process design.) However, today's document-based processes and offline design tools make it challenging for pharmaceutical manufacturers to maintain a so-called "single version of the truth." Thus, a rigorous *digital* process design should form the core of the process knowledge framework.



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With true Process PLM, digital process design provides the framework for integrating the entire product lifecycle, centralizing knowledge management and automating information sharing across systems.

That was Neo PLM's vision when we developed the industry's first digital process design and simulation tool that integrates directly with existing systems including Manufacturing Execution Systems (MES), Distributed Control Systems (DCS), data historians and even Enterprise Resource Planning (ERP) systems. Finally, pharmaceutical manufacturers have an application analogous to CAD—the technology that revolutionized the discrete industries.



Within the context of the ISA 95 framework, Process PLM will serve as an integration layer that unites the others around a digital definition of the process.

The process design can then serve as a powerful framework to connect all aspects of the product lifecycle:

- 1 Production planning** – Manufacturers can easily compare the impact of different processes and production scenarios to determine how to make the highest quality product at the lowest possible cost, with the least environmental impact. Greater visibility into scheduling enables CMOs to maximize their asset utilization.

- 2 Configuring shop-floor systems** – No more inefficient, error-prone manual processes. No more knowledge loss during technical transfers. CMOs can more quickly begin manufacturing new products, or change over from one product to another.

- 3 Production data analysis** – Execution data can be automatically mapped back to the design, making it much easier to verify the recipe is being executed according to plan.

The end result: Timely data analysis informs process improvements and other business decisions, creating a closed loop—the “holy grail” of manufacturing integration. On the drug development side, scientists can focus more on their core work and less on documentation requirements.

4 Steps for Getting Started

That vision for the future of pharmaceutical manufacturing sounds incredibly exciting, you say—but implementing a PLM solution seems daunting. It doesn't need to be.

First of all, PLM technology isn't necessarily a single enterprise system. Rather, it ideally serves as the “glue” connecting different stages of the product lifecycle. The Neo PLM solution, for example, is a suite of modules that sit between systems in your existing technology architecture—with design at the center.

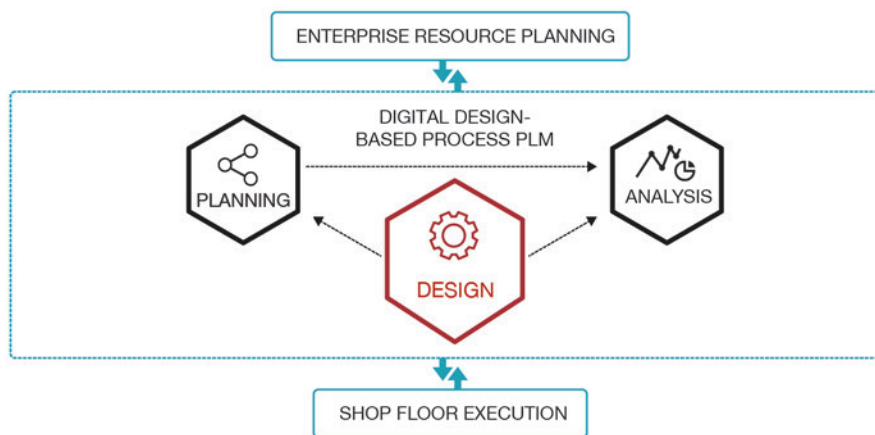
Ultimately, of course, unifying the entire product lifecycle will impact virtually all functional areas and require significant business process re-engineering. However, with a modular solution, integration can occur in a phased manner with capabilities added incrementally until the manufacturing loop is closed:

PHASE 1 It all starts with a comprehensive digital process design tool that can communicate with your current systems. (Implementation can be relatively inexpensive.) Deploy the technology in Process R&D and at your manufacturing sites—both internal and CMO—and you have the foundation for radically transforming technical transfer.

PHASE 2 Building on that foundation, you can implement PLM technology that integrates with your digital design tool to provide a comprehensive, end-to-end view of production scenarios for a product, enabling easy comparisons.

PHASE 3 Production planning technology can be integrated with your design tool and production scenario browser, providing rich data to your ERP system and giving you a globally integrated platform for managing product supply.

PHASE 4 You can now close the loop by deploying process analysis technology that integrates with both your shop-floor systems and design and planning software. The result: unprecedented insight to support critical business functions such as batch review and release and process optimization. These capabilities can be extended across the enterprise, enabling a new paradigm for production technical support and troubleshooting.



Process PLM can be implemented in phases as the “glue” that connects your current systems, ultimately closing the manufacturing loop.

Conclusion: Time for a 21st Century Solution

It has been more than 30 years since the seeds of radical change took hold in discrete manufacturing with the advent of CAD—which, in turn, enabled the introduction of transformative PLM technology. Well over a decade has passed since the FDA launched its “21st Century” initiative encouraging drug makers to modernize their technology. Now it seems the time has finally come for the pharmaceutical industry to undergo the sort of technological revolution once seen in the discrete world.



Digital design-based PLM technology connecting every step in the product lifecycle—and closing the manufacturing loop—represents the future for pharmaceutical companies for two main reasons:

- Industry conditions have changed significantly in several key areas in recent years, rendering document-centric approaches unsustainable.
- The foundational technology finally exists in the form of a digital process design tool that integrates with manufacturing and resource planning systems.

At last, all stakeholders—from scientists to process engineers to CMOs—can be united around a “single version of the truth.” That seamless information sharing can streamline and accelerate manufacturing while enabling ongoing process and business optimization. Both product quality and profit margins can be improved as a result. Ultimately, with scientists liberated from paperwork burdens, today’s document-based approach will give way to a new paradigm—focused on science and innovation rather than documentation.

Citations

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