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REVIEW ARTICLE

Product Lifecycle Management (PLM): A Challenge in Pharmaceutical Industry

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ABSTRACT

One meaningful and holistic approach to today's current challenges within the pharmaceutical industry is to focus on Product Lifecycle Management (PLM), which is a business transformation approach to manage products and related information across the enterprise. PLM, as the term might imply, is the implementation of optimization strategies as the product goes through the traditional development and marketing pathway, in order to harness the total value of the product during its market journey. The life cycle refers to the period from the product's first launch into the market until its final withdrawal and it is split up in phases. It is a highly evolved approach, especially in competitive industries such as Fast Moving Consumer Goods and electronics, and has been instrumental in sustaining many big brands. The evolving nature of the pharmaceutical industry, not to mention a more competitive business climate, has fuelled interest in the discipline of PLM as a way of sustaining growth and profitability in the pharmaceutical industry. But while the industry has realized its importance as an area of investment in the last couple of years, adoption has been lackluster, with poor senior management commitment and a lack of clarity on the basic rationale for implementation. The pharmaceutical industry is going through a period of transformation where defining the value of a product is becoming more and more important. If you look at all major areas of contention between stakeholders, there's one dominant theme: the perception of value has taken the centre stage in current business environment and the products which can clearly define and communicate that value will eventually thrive. The only way pharmaceutical companies can create and communicate value is by taking an early and a proactive approach towards deciphering the journey of the product from its initial stages in the laboratory to the end of patent life and beyond. The rapid pace of change in the industry is something that pharmaceutical companies have often been slow to adapt to. Payers and regulators hold a very different perspective to pharmaceutical companies about the value of a product in a particular therapeutic area. The only way to bridge this value perception gap would be to start early and engage effectively at every level of the life cycle of the product whilst identifying core strength and weaknesses to fully capitalize on the market opportunity. This review rectifies the information about the needs and importance of PLM.

KEYWORDS

Product Lifecycle Management, Pharmaceutical Industry, Profitability, Therapeutic Area

INTRODUCTION

All products and services have certain life cycles. During this period of Lifecycle Management (LCM) significant changes are made in the way that the product is behaving into the market i.e. its reflection in respect of sales to the company that introduced it into the market. Since an increase in profits is the major goal of a company that introduces a product into a market, the product's life cycle management is very

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important. Some companies use strategic planning and others follow the basic rules of the different life cycle phase that are analyzed later[1].

The pharmaceutical industry currently faces marked challenges in its long-standing business model. PLM is being used to maximize the revenue-generating potential of pharmaceuticals, especially in their maturity. Pharmaceutical Product Lifecycle Management 2010-2020 - the PLM strategies are examined that pharmaceutical companies are using .which ranges from reformulations, new combinations of drugs and expanded indication ranges, to the use of alliances, licensing, mergers and acquisitions. The interface between Research and Development (R&D), marketing & sales, product & brand management, pricing, distribution, retailing and promotional issues within the pharmaceutical industry are the important target for the pharma industry. Relationship of product management with other functions like sales and marketing, pre-marketing awareness launch planning, budget setting and allocation of resources for promotions are main highlights of the course. The course will also focus on the marketing research process and steps involved in a marketing research study. While the primary emphasis will be on the Indian pharmaceutical industry, attention will also be paid to the Global Pharma Industry[2].

In recent years the pharmaceutical industry has faced declining R&D productivity, a rapidly changing healthcare landscape and fierce competition from generics resulting in lower growth and profit margins. Historically, drug development focused on clinical trials management and outcomes. Now however, the industry is looking at more holistic approaches to improve processes of bring new products to market that can accelerate product development while lowering operational costs. This is challenging because of the complex value chain and business processes required in this highly regulated environment. Additionally, it has proven difficult for the industry to effectively adapt as many pharmaceutical companies are simply not optimized for cross functional collaboration which is so desperately needed to support these changing market conditions.

One meaningful and holistic approach to today's current challenges within the pharmaceutical industry is to focus on PLM, which is a business transformation approach to manage products and related information across the enterprise. In recent years PLM has provided many pharmaceutical organizations with the ability to increase their ability to get products to market quicker, ensure greater regulatory compliance and efficiencies while reducing development costs[3].

Figure 1: Product lifecycle management

Product Life Management includes the following Technical Activities

Pharmaceutical Development

- Drug substance development
- Formulation development (including container/closure system)
- Manufacture of investigational products
- Delivery system development (where relevant)
- Manufacturing process development and scale-up
- Analytical method development
- Technology Transfer

- New product transfers during development through manufacture
- Transfers within or between manufacturing and testing sites for marketed products
- Commercial Manufacturing
- Acquisition and control of materials
- Provision of facilities, utilities, and equipment
- Production (including packaging and labeling)
- Quality control and assurance
- Release
- Storage
- Distribution (Excluding wholesaler activities)

Product Discontinuation

- Retention of documentation
- Sample retention
- Continued product assessment and reporting[2]

Drug Life Optimization[4]

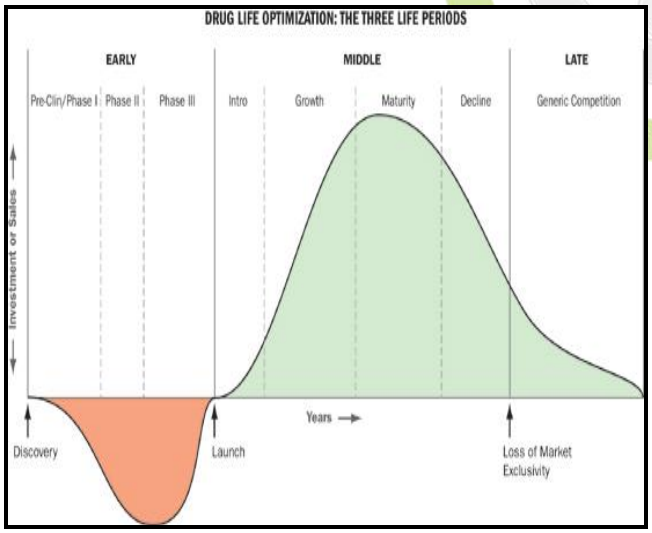

Figure 2: Drug Life Optimization enables pharmaceutical professionals to view the entire life not just the lifecycle of a product and to make more appropriate, timely, and strategic decisions to maximize cumulative, lifetime sales, represented as the area under the curve in green. Source: Stan Bernard, Bernard Associates, LLC, 2013

Statement of the Perceived Problem

There is currently a lack of a harmonised approach on technical and regulatory considerations for lifecycle management. While the concepts in International Conference on Harmonisation ICH Q8, Q9, Q10 and Q11 provide opportunities for a more science and risk-based approach for assessing changes across the lifecycle, several gaps exist which limit full realization of intended benefits. The envisioned post-approval 'operational flexibility' has not been achieved. The main emphasis at ICH to date has focused on early stages of the product lifecycle (i.e., development through launch).

A similar focus is now needed for the commercial manufacturing phase in order to fill the gaps in the implementation and fully realize the opportunities promised by ICH Q8 to Q11. For example, lack of alignment has led to confusion on the necessary information and level of detail in the dossier and its impact on change management and regulatory reporting. The lack of harmonized approaches for technical and regulatory aspects for lifecycle management can hinder innovation and continual improvement in the pharmaceutical and biotechnology sectors.

In addition, there is an inconsistent utilization of post-approval change management plans and comparability protocols. As a consequence, opportunities to prospectively manage future changes in a more strategic manner, particularly where there is enhanced product knowledge and process understanding, have not been fully realized[5].

Life Cycle Management (Reformulation and Drug Repositioning)

Life Cycle Management is no-longer just about reformulation of existing drugs with only incremental performance improvements. In the current climate of evidence-based medicine and cost containment physicians and payers demand significant enhancements in performance or the answer to unmet medical needs in order to justify prescription or reimbursement.

Oral Modified Release

Case Study

The Challenge

Many patients with rheumatoid arthritis (RA) experience morning stiffness, the duration of which is strongly associated with functional disability, pain and general patient health. The duration of morning stiffness has been identified as the second-leading predictor for change of disease modifying drugs or biologic therapy. Prednisone is an established treatment for RA, but the traditional regime of morning administration does not mediate the nocturnal cytokine peak, so patients can experience stiffness and pain for several hours after treatment.

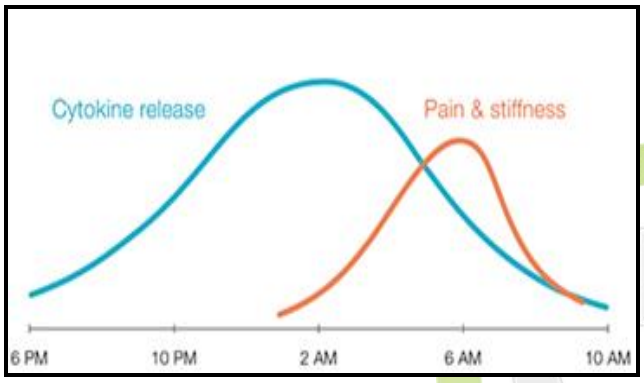

Figure 3: Cytokine release and Incidence of Pain with traditional Regime of Morning Drug Administration

The Solution

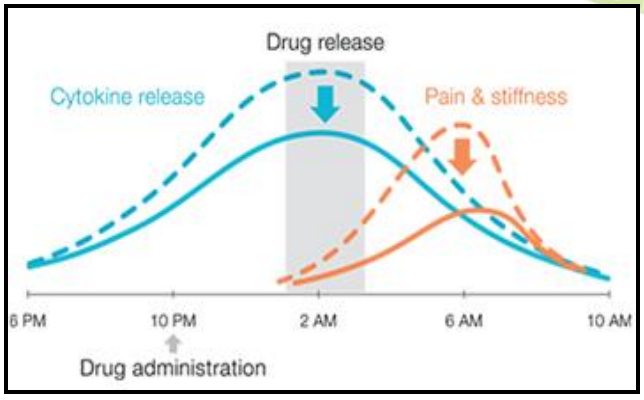

Figure 4: Chronologically Designed Prednisone Coinciding with Cytokine peak and decreases the Morning Pain

Skyepharma formulated the RA drug prednisone using its' GeoclockTM chronotherapy so that the active drug is released with a lag-time of 4 hours after bedtime dosing in order to coincide with the night-time cytokine peak, and so reduce early morning stiffness the repositioned product (Rayos® in the US/Lodotra® in Europe) is marketed by Horizon Pharma. It has been granted a premium price andreimbursement[6].

Challenges in Pharmaceutical Product Life Cycle Management

- Increasing Internal and External Complexity
- No Single Data Source for Products and Related Information
- Research and Development Improvement
- Technology Transfer
- Integrated Quality and Risk Management
- Comprehensive Packaging
- Global Product Registration
- Intellectual Property Portfolio
- Managing Complex Collaborative Outsourcing Networks.
- Corrective and Preventive Action (CAPA) System
- Burden of Systems Validation[7]

Issues that are Integral to Product Lifecycle Management

In order to properly conduct the many activities related to lifecycle management, leaders must fully understand the main issues that are integral to lifecycle management. From regulatory changes, to expanding into emerging markets, the lifecycle management process is constantly shifting.

- ***Regulatory Changes Expected to Impact Lifecycle Management*:** All five of the most often used LCM strategies are expected to be weakened by regulation / reform over the next 12 months. These strategies tactics include: new dosage form, publication strategies, new dosing regimen, new indication and strategic pricing.
- ***Emerging Markets Play a Lead Role for Many Organizations*:** Almost 80% of companies seek to expand into emerging /

developing markets, seeing this as a strong late-life tactic. In fact, this strategic goal was considered to be one of the most effective means of deriving value from late-life brands.

- ***Barriers to Use are high*:** Across all strategies, the length of time required to execute was the most frequently cited barrier to use for any LCM strategy examined.
- ***Create a Mature Brand Organization*:** Create a centralized group to focus on LCM. By creating a mature brand, companies streamline operations and decision-making, which helps with setting lifecycle[8].

Specific Recommendations

"There are two essential building blocks: first, fast transfer from R&D to manufacturing, and second, linking feedback from patients directly to the development and manufacturing process," says Maes. Many of these changes cannot wait. Regulators are now requesting insight on produced batch information. Data information systems need to be configured to allow safe and efficient data exchange with authorities and clients.

In the other direction, feedback from clients and suppliers offers opportunities for product improvement. Internet portals and customer relationship management (CRM) systems must be developed to capture this feedback.

Judging the Best Technological Moves

Many companies seek to implement change but do so in ways that do not maximize benefits. To better accommodate the forces that will shape the future of pharma, road maps should cover 5 to 10 years. In the short term, companies will upgrade facilities to lower manufacturing costs, increase safety and quality, comply with new regulations, and so on. These upgrades can include more automation, integration of equipment and systems, and new technologies. In the medium term, companies will increasingly replace batch manufacturing and "after the event" product testing with automated and integrated continuous manufacturing. This will allow manufacturing on a smaller footprint. And finally, in the long term, more personalized medicines could increase manufacturing and supply chain complexity. A larger variety of products will require greater flexibility in production and closer integration along the whole pharmaceutical chain[9].

Large gap between R & D Operational Performance and Strategic Importance

To address the development process, the pharmaceutical industry has identified key R&D functions that are considered important in optimizing R&D pipeline effectiveness (AMR). This research indicates significant gaps exist between R&D operational performance and strategic importance resulting in the industry operating at less than 50% effectiveness and how a poor capital allocation lead to decline in pharmaceutical R&D innovation[10].

Table 1: Pharmaceutical Product Life Cycle Management and Portfolio Management

Phase I	**Discovery** Identify new drug targets and high-quality drug candidates Leverage previous research and intellectual property Use collaborative research networks
Phase II	**New Product Development** Manage patent applications Manage clinical production processes Collaborate on and corroborate clinical trial results Prepare and peer review internal results reports Leverage preferred contract research organization (CRO) identity
Phase III	**Regulatory Submission and Approval** Aggregate documentation for regulatory submission and archiving Manage nondisclosure agreement submittal and approval process Manage facilities inspection process Prepare for technology transfer

Phase IV	**Product Launch** Coordinate sales, marketing and production activities to hit launch date. Execute technology transfer Gear up for new product supply
Phase V	**Commercialization** Manage full-scale production, packaging, and labeling Rely heavily on chief medical (CMOs) and chief pharmaceutical officers (CPOs) Maintain cure Rent Good Manufacturing Practice process and documentation compliance Manage direct material costs including packaging and labeling.
Phase VI	**Quality Management** Maintain and manage standing operating procedures (SOPs) and quality assurance (QA) systems Conduct continuous internal and external supplier audits Execute continuous closed-loop corrective and preventive action (CAPA**)** management
Phase VII	**Phase-Out and Extension** Prepare to battle generic competition Prepare for drug line extensions Continue maintenance of documentation in case of adverse events[11].

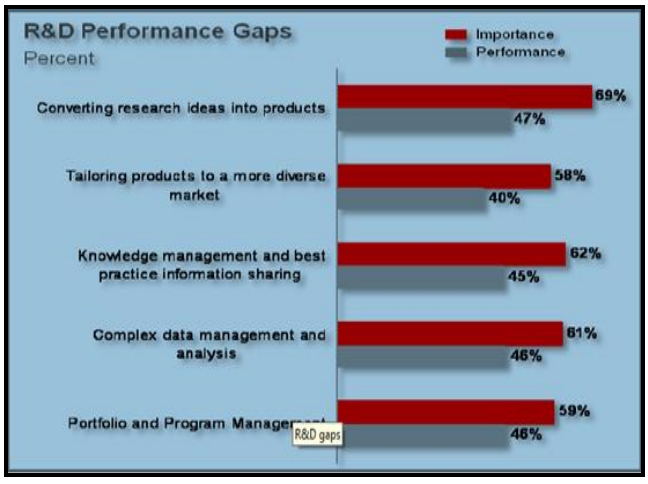

Figure 5: R&D Performance Gaps

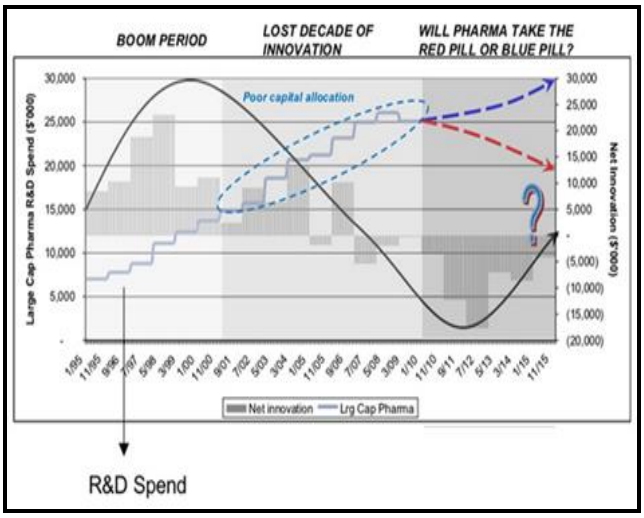

Figure 6: Poor capital allocation leading to decline in pharmaceutical R&D Innovation

Table 2: Next generation of PLM solutions

Trends	Description
1. Integrated capabilities	Capabilities are becoming more integrated in PLM. An engineering Computer-Aided Design (CAD) system and a manufacturing simulation system can share information. Design and simulation can feed information to each other. For instance, engineering can integrate finite element analysis with geometry, analysis tools are built-in.
2. Moving further into the lifecycle of a product	PLM is moving further into the lifecycle as it was defined to begin with. Companies are kitting out their products with instruments that can provide real-time feedback on the product as the customer is using it. This will decrease or eliminate the need for surveys and warranty repair data, which has traditionally informed companies how their product is performing.
3. Enabling technologies	"Cloud computing is really the same computing we've had," Grieves says. "We just

	don't know where the servers are." The hardware exists already, but it's the virtualization that is key. Cloud technology allows organizations to buy software as a service rather than having to worry about putting up a server to service the application. In this respect, Grieves argues, distributive computing changes the model of how software gets sold.
4. Integrating the supply network	PLM has traditionally existed within the four walls of an organization and information tends to get stuck there. Now we are seeing an interest in integrating the supply network within the PLM system, making cloud computing easier. Grieves predicts that this will raise privacy and security concerns, but ultimately these are technological problems which can be worked through and solved.
5. Mobile technology	Grieves gives a great example for this one: what if we could stand next to an airplane and point a mobile at it and it shows us the inside of the plane so we know which access panel to open? Augmented reality has great potential and goes beyond simply looking at information on a screen. Eventually, displaying virtual information on top of a physical object will be the norm[13].

Market trend/Challenges

Phlegmatically evolved Product Data Management (PDM) in Pharmaceutical Industry

(i) Pharmaceutical domain does not have standardized product data modeling software and collaborative electronic data managed like CAD software.

(ii) Some of the companies in Pharmaceutical domain are using PLM for product portfolio management & art work and packaging.

(iii) PLM products are still need to evolve for managing pharmaceutical product design data and act as collaborative platform within internal departments across the enterprise and with external groups.

Smaller Companies Cannot Afford Cost of Implementation

(i) Pharmaceutical domain specific solutions are available at very high cost.

(ii) This investment is huge for a small biotech companies. One of the solutions for this could be using the open source PLM platform.

(iii) The vendors of these solutions and also current PLM product market leaders have to come up with lighter version of the solutions with pharma specific processes.

Pharmaceutical Industry is mischarged for Unrelated Engineering Complexity

(i) Pharmaceutical Industry involves totally different type of complexity world which could be related to physical and chemical complexity, storage, shelf life related complex problems.

(ii) Current PLM products are much evolved to handle engineering complexities and hence the cost is also in proportion to the engineering complexities solved with PLM.

(iii) The PLM vendors should have domain specific costing.

Less Matured Pharmaceutical Domain Specific Processes in PLM Space

As earlier stated PLM has started its journey from automotive/aerospace products and then embraced by pharmaceuticals, it is just a matter

of time for PLM to evolve and become mature enough to cater the needs to industry.

Table 3: Pharmaceutical Product Lifecycle Management Strategies: Used to extend the life of drug

1.	Name brand (Innovator) pharmaceutical companies must extend the product life cycles of drugs to maintain profits, exclusivity, market share and transition into next generation products.
2.	Patent protection is crucial to the innovative pharmaceutical industry.
3.	Innovative companies require the guaranteed period of market exclusivity to sustain drug prices, recoup research and development costs and to fund the development of new products or next generation drugs.

Table 4: Consideration for the pharma product manufacturing

1.	Is there something within the tablet such as a component (excipient) that imparts a unique characteristic to its performance? This could be a unique method of targeting a specific binding location or target selection site in the body. An example of this could be to coat an uncoated tablet with a functional coating system that would impart a greater degree in precision in targeting the area in the gastric system to increase the bioavailability to the blood stream and thus creating a more effective product. Targeting sites for better bioavailability can also lead to decreasing the dosing regimen for a potentially safer, more efficacious product.
2.	One may examine the potential of over-encapsulating a tablet product to change the delivery system of the drug product.

CONCLUSION

The complexity of today's pharmaceutical market requires more efficient drug development and production. PLM has the opportunity to make pharmaceutical production more effective and with lower risk even in this vastly complex environment. The product lifecycle management creates and manages a company's product-related intellectual capital starting from an idea to its final retreat. In pharmaceutical industry, it benefits through enhancing the lifespan of patent and pricing strategies. The Agile Product Lifecycle Management platform is designed to address pharmaceutical companies' most pressing business issues including speeding time to market, reducing operating and product costs, achieving high-quality standards, and providing product governance and compliance with regulatory agencies.

REFERENCES

1. Komninos, I. (2002). Product life cycle management. *Innovation*, 1-27.
2. *Guidance for Industry Q10 Pharmaceutical Quality System*. Available from: http://www.fda.gov/downloads/Drugs/Guidances/ucm073517.pdf
3. Todd Hein. *Product Lifecycle Management for the Pharmaceutical Industry*. Oracle Life Sciences.
4. http://www.learnpharmascience.com/tablet-apps/ebook4-trialcard/issue4.pdf
5. *Final Concept Paper Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management*. Dated 28 July 2014. Endorsed by the ICH Steering Committee on 9 September 2014.
6. Life Cycle Management. Reformulation and Drug Repositioning Available from: www.skyepharma.com/.../Skyepharma-LifeCycleManagement.pdf.
7. Challenges in Pharmaceutical Product Life Cycle Management. Available from: http://www.askaboutgmp.com/50377-challenges-in-pharmaceutical-product-lifecycle-management#
8. Best Practices, LLC blog World-Leading Business Benchmarking Research & Consulting Firm. http://whybenchmarking.com/

9. http://www.industry.siemens.com/topics/global/en/magazines/process-news/pharmaceutical/pharmaceutical-trends-pharma-2020/pages/default.aspx
10. Sethy, S. P. Tahseen Sameena, Patil, P., Shailaja, K. Product lifecycle management in Pharmaceuticals: A Review. *Pharma tutor*.
11. *Product Lifecycle Management in the Pharmaceutical Industry*. An Oracle White Paper Updated January 2008.
12. http://www.pharmatutor.org/articles/product-life-cycle-management-in-pharmaceuticals-review?page=0,1
13. 5 Trends in Next generation PLM. Available from: http://blogs.ptc.com/2012/01/26/5-trends-in-next-generation-plm/

