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Mitigating the Fall

Branded pharma strategizes to stay profitable despite expiring patents

By Karen Langhauser, Chief Content Director

EVEN THOUGH the pharmaceutical industry is approaching what most analysts say is the tail end of the patent cliff tumble, the industry is still under pressure to develop strategies to stay profitable in what looks to be a new, non-blockbuster-reliant era.

In the shrinking window between market approval and patent expiration, pharmaceutical companies are coming face to face with the stark realties of revenue erosion. In the United States and Europe, generics — strongly incentivized by payer initiatives — are here to stay, making the strategies brand pharmaceutical companies employ both before and after patent expiration imperative to fiscal survival. In worst-case scenarios, once drugs lose patent protection, generics can erode up to 90 percent of branded drug sales. According to IMS data, by 2020, only 18 percent of traditional drug volumes in developed markets will consist of original branded pharmaceuticals, and 8 percent volume in emerging markets[1].

2016 will see numerous high-profile drugs going off-patent, as more than two dozen major pharmaceuticals take the plunge off the patent cliff. According to EvaluatePharma data, between 2015 and 2020, a total of $197 billion sales are at risk from patent expiries, but the market currently predicts that only $99 billion of this will actually materialize[2].

Financially speaking, the good news for the pharmaceutical industry is that prescription (both branded and generic) drug sales continue to rise. EvaluatePharma predicts that the market for prescription drugs, based on consensus forecasts for the leading 500 pharmaceutical and biotechnology companies, will grow by 4.8 percent per year to reach $987 billion by 2020.

Branded pharmaceutical companies have been employing a combination of strategies, often concurrently, to retain market share once generics come into play. Forward-thinking companies have adjusted their business strategies, finding ways to turn dreaded patent expirations into opportunities to innovate and bring new value to patients and populations.

MARKET PROTECTION FUNDAMENTALS

At the most basic level, drugs have two forms of market protection in the U.S. — exclusivity and patent protection. Patents, granted by the U.S. Patent and Trademark Office, generally have a term of 20 years from the date of filing. Beyond the initial patent filings, which pro-

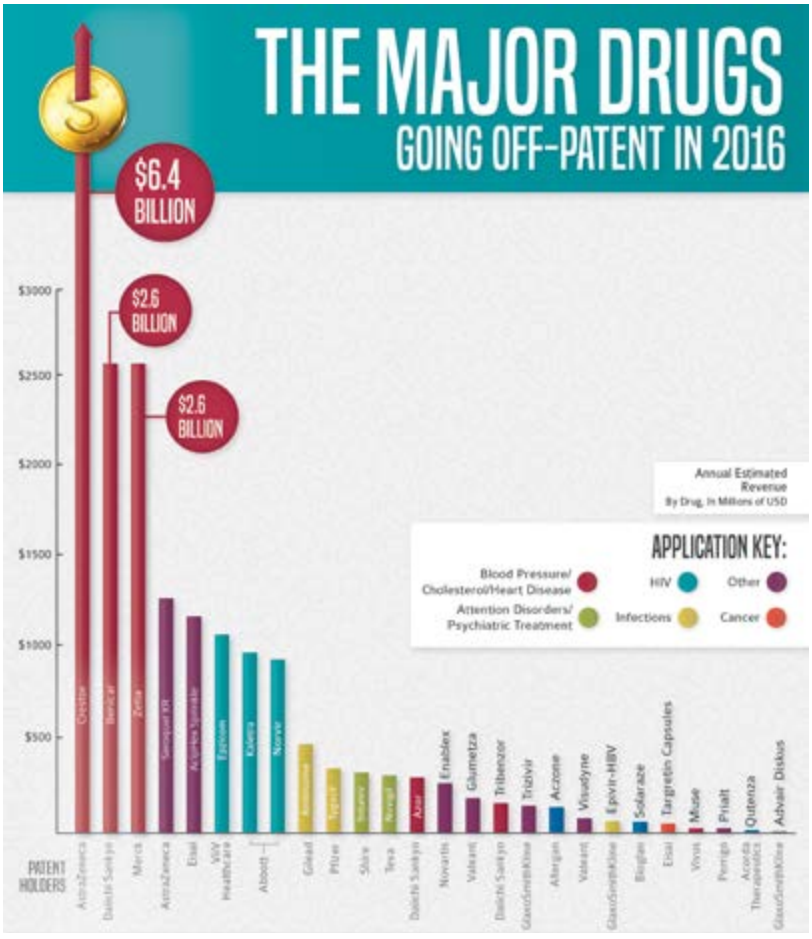
tect compositional matter of a new chemical entity, secondary or "follow on" patents can be sought to protect improvements to, additional discoveries through scientific data, or new uses for the pharmaceutical not suggested in the original patent.

Peter Knauer is chief regulatory officer for ARC Experts, a leading consultancy offering specialized services to the pharma, medical device, diagnostics and biotech industries to assist with regulatory, compliance, audits and all risk related issues. Knauer, a veteran of nine successful NDA/BLA approvals, explains, "There is essentially a 'porfolio' of patent opportunities that come with each product, so manufacturers can extend patent life years beyond initial patent. But eventually, even that runs out, so where do you take it from there?"

The answer to that for many manufacturers often lies in exclusivity. Given the complexity and length of the drug approval process, there is often little patent protection left on a product by the time the drug hits the market. To provide pharmaceutical companies with a fair chance to recoup R&D investments and incentivize continuing innovation, the Food and Drug Administration offers numerous exclusivity provisions to drug manufacturers. The FDA cannot legally approve a generic drug application for that product until the exclusivity period expires.

"There are unique opportunities that can offer additional and extended exclusivity to encourage a pharmaceutical manufacturer to go after smaller markets, and getting this exclusivity can be very lucrative for a company," says Knauer.

One trend that continues to gain favor, according to Knauer, is seeking orphan drug exclusivity. Targeted at diseases with high unmet medical needs, orphan drugs have the potential to receive faster approval from the regulatory agencies and higher levels of reimbursement. Companies can request orphan-drug designation of a previously unapproved drug, or of a new use for an already marketed drug — breathing new life into an already existing product.



If a product is granted orphan drug exclusivity, FDA may not approve applications for generic products that contain the same active ingredient and are labeled for the same orphan indication for seven years. The market for orphan drugs, according to EvaluatePharma's 2015 Orphan Drug Report, will grow by 11.7 percent per year between 2015 and 2020 to reach $178 billion. And, according to the report, "large pharma groups finding orphan indications for some of their biggest sellers mean that seven of the 10 top companies by orphan indications are global majors."

STRONGER FOCUS ON LIFECYCLE MANAGEMENT

The post-blockbuster era has led to a fundamental shift in how pharmaceutical manufacturers structure their organizations, with more attention being given to the optimization of existing branded drugs. The majority of branded drugmakers now have dedicated business units for managing established products.

According to Simon Goeller, a partner at McKinsey & Company, "In the past, pharma was so focused on new compounds that they didn't pay much attention to the value proposition of existing compounds. A combination of the loss of blockbuster revenue and waning pipelines has resulted in

pharmaceutical companies focusing a greater deal of attention towards optimizing later lifecycle products and putting dedicated resources behind managing these more mature molecules."

In 2008, Pfizer took the lead in this initiative by completely reorganizing its pharmaceutical segment into customer-focused business units — one of which was devoted specifically to established products. According to Pfizer's 2008 Annual Report, "Established Products is taking a previously shrinking segment of Pfizer's business and transforming it into an engine of growth through creative product enhancements, the licensing of additional products, and the promotion of Pfizer quality and customer care."

Extension strategies such as reformulating drug delivery or finding new indications are common in pharma lifecycle management. Critics of pharma lifecycle management often cite reformulation in the "evergreening" debate, claiming that drug companies are more focused on their own economic value than the therapeutic value these extensions bring to patients. Recent political focus on drug pricing has seen policy makers pushing the FDA to target exclusivity periods to only the truly innovative products, rather than drugs that are minimally different from existing ones.

As a result, many branded pharma manufactures are re-evaluating their product lifecycle management strategies in order to best maximize products still under patent protection and provide true patient value. According to Goeller, "Which lifecycle management approach companies take always depends on how they feel they can best build a value position in the market. To be successful, manufacturers need to offer product extensions that bring true clinical benefits that improve the quality of life for patients."

Catalent, for example, is helping its customers develop new drug-delivery formats that overcome a major formulation obstacle — poor solubility. Solubility is one of the most frequent culprits of poor bioavailability and limited drug absorption. According to Chris Halling, senior manager of global communications for Catalent Pharma Solutions, "Solubility of existing drugs is an issue that is often overlooked in favor of developing new drugs." Catalent has extensive experience converting existing formulations into other forms such as softgels, which may offer a solution to solubility challenges, as well as patent benefits and numerous patient experience benefits. Softgels are perceived to generate a faster onset of action, can reduce API dose and side effects, and improve overall treatment performance. Additionally, softgels encourage compliance, as they are sometimes easier to swallow, appealing to specific patient groups, such as the elderly.

These newly realized benefits become extremely important when looking to product lifecycle management as a patent extension strategy. Echoing the sentiments of Goeller, Halling says, "It is not worth doing unless you can truly differentiate your product and show patients a genuine brand value."

BETTER LATE THAN NEVER?

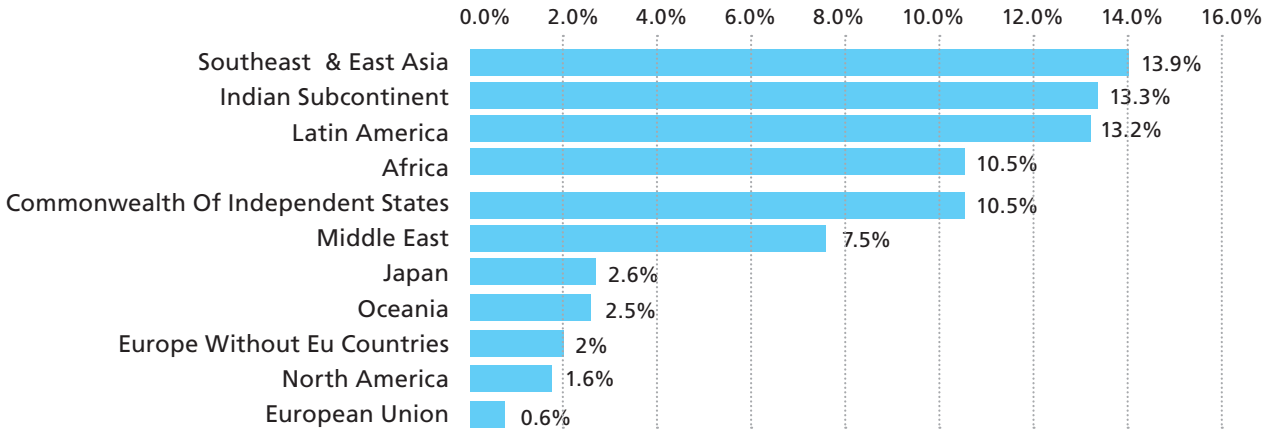
It is universally acknowledged that a crucial component of product lifecycle management in general is timing — establishing a plan for patent expiration mitigation early in a product's lifecycle. The unfortunate reality is that this rarely happens.

The extensive and exhausting process involved in getting an initial drug approval as well as managing existing products oftentimes means anticipating the patent expiration from the drug development stage is little more than "wishful thinking."

"Today's pharma companies are operating lean and are busy nurturing existing products and managing risk strategies," says Knauer. "As such, being able to not only plan, but then strategically implement forward thinking product lifecycle extending or enhancing plans is challenging." Knauer has offered several ideas around dovetailing improvement and enhancement of intellectual property and patent management plans:

1. More transparent licensing or grant options on the existing library of compounds, with exclusivity, to boost innovation and speed the process of drug discovery and development.

Projected global pharmaceutical market growth from the period 2011-2016, by region (CAGR)



Source: IMS Health

Projected global pharmaceutical market growth for the period from 2011–2016, by region

2. More comprehensive and deeper understanding of all international regulatory compliance additions and changes.

3. Development of collaborative academic-to-industry relationships to boost innovation and Intellectual Property generation.

4. Assess potential of emerging markets early, i.e., China, India, Middle East, Africa to understanding their challenges, demographics, specific diseases and resources available.

5. Encouraging patent reform, by working with foreign patent authorities in developing countries, for protection of their products through patent exclusivity enforcement.

Some pharmaceutical companies are finding ways to get ahead by researching extension options well in advance of patent expirations.

Novo Nordisk, for example, is looking to minimize loss after its blockbuster injectable type-2 diabetes medication, Victoza, loses patent protection next year. Novo is approaching commercialization of replacement biologic, semaglutide and recently announced results from the last global Phase 3a trial. Semaglutide is a once weekly injectable for the treatment of type II diabetes. Novo recognizes, like many branded pharmaceutical manufacturers, that reformulation of injectables into orals can extend the lifecycle value of existing molecules. Already ahead of the game, Novo is simultaneously developing a long-acting oral version of semaglutide intended as a once-daily tablet treatment for the same indications as the injectable version. Currently, GLP-1 receptor agonists are available only as injectables.

OUTCOMES-BASED APPROACH

With the upcoming presidential election, drug pricing ranks high are on the country's radar. Value-based pricing models for pharmaceuticals — the concept of requiring data comparing various treatments to help reach a "fair" price — have become an extremely popular idea amongst political policy makers. The Value Based Pricing System (VBPS), which has been adopted in the UK for branded drugs sold to the National Health Service, looks to set the price of a drug based on the benefit it brings to the patient and the healthcare system and will only reimburse drugs that provide true value to patients.

The definition of "value," however, is subjective and varied, making this a difficult model to adopt. What can be derived from this, though, is the idea that drug pricing should have a close relationship with the drug's ability to deliver results. Though the idea is still in nascent, some branded drug manufacturers are responding to this call-for-action by experimenting with pay-for-performance models tied to a treatment's effectiveness rather than simply the volume of drugs sold. These drugmakers are putting resources in place from the start of the process to ensure molecules are developed in a way that truly delivers value, in order to counteract the limited days of the blockbuster.

In 2013, Novartis CEO Joseph Jimenez spoke candidly about how he navigated Novartis through the loss of patent protection on its best-seller, Diovan[3]. Said Jimenez

in a Wall Street Journal interview, "I really believe that in the future, companies like Novartis are going to be paid on patient outcomes as opposed to selling the pill." Though Jimenez has recently addressed the obstacles Novartis faced when trying to implement an outcomes-based plan for its heart drug Entresto, Jimenez is still supportive of a future industry shift away from a transactional approach to pricing and selling drugs.

Amgen saw better success with its outcomes-based approach taken with pricey cholesterol drug, Repatha, approved by the FDA in mid-2015. Amgen linked the net price of Repatha to expected LDL cholesterol reductions and anticipated appropriate patient utilization. Unique to the deal that Amgen set up with insurers is that Amgen will have to provide larger rebates to payers if patients' cholesterol levels are not lowered to levels observed during clinical trials.

An outcomes-based approach has the potential to make insurance companies and government payers more willing to approve reimbursement for new drugs, as well as help drugmakers to differentiate their pharmaceuticals against competitors through higher value achievement.

EMERGING MARKETS

According to McKinsey analysis, between 2015 and 2020, emerging pharmaceutical markets are expected to account for $190 billion in sales growth[4]. Generics play a pivotal role in these markets. "Sometimes the solution comes down to geography. Generics behave differently and have different regulations in emerging markets," notes Goeller.

While entering the unbranded commodity generics market in the U.S. — where generics are sold at the lowest possible price and most consumers cannot distinguish one manufacturer from another — is not vastly appealing to branded pharma; generics in emerging markets such as Russia or China offer more potential.

"The U.S. has rapid generic erosion, whereas in many emerging markets the originators are better able to retain market share," says Goeller.

In these countries generics are typically sold as branded products — sometimes for as much as 80 percent of the original price. These markets are often plagued with quality issues, resulting in consumers who are more likely to opt for generics that carry the name of a trusted manufacturer.

Despite existing obstacles surrounding healthcare infrastructure and IP protection, branded pharmaceutical companies are recognizing the value in these emerging markets, and customizing their strategies in order to create a product that is accessible to the masses and yet profitable at the same time.

As the pharmaceutical landscape changes, branded drugmakers are shifting their focus from big money blockbusters to strategies that increase returns from already approved drugs, before and after patents expire. What's old can in fact be new again, and in some cases, yield more effective treatments and meet the unmet medicals needs of a wider population.

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PLM for Pharma: Applying an Old Tool in New Ways

How pharma companies are tapping into the capabilities of Product Lifecycle Management tools to address the product and process data challenge

By Chris Albani, Vitaly Glozman, Wayne McDonnell, Shankar Iyer and Yun Wakana Wang, PwC

DR. SMITH — the development lead for her company's most promising new drug product — has been losing sleep over the past month pulling together the CMC (Chemistry, Manufacturing and Control) section of the regulatory submission. The compound has shown excellent efficacy and safety data, and the entire company is counting on a quick review and approval. Dr. Smith is now faced with a significant headache, though. She is searching for key information related to solubility that was characterized early in development. She had to email, call and even physically visit the medicinal chemistry team. While she has been successful with most of the data, results from one series of tests is proving hard to find. The individual responsible for the tests long ago left the company and now no one knows where to find the missing information. Dr. Smith knows that re-running the tests would be risky — and might even delay the filing — so she is now in a manual process to hunt down the data across multiple databases.

This is an issue commonly heard across pharma companies. While this specific example occurs in CMC, similar problems happen in many of the other functions. As pharma companies are becoming increasingly lean, new processes and technology approaches are needed to move our scientists, engineers and specialists away from documentation management and back to their core skill set.

NEW APPROACHES AND TOOLS FOR A CHALLENGING LANDSCAPE

Recent years have brought tremendous change to the pharma landscape. Significant economic pressures are driving an increased focus on costs within healthcare systems and payers around the world are under increased pressure to deliver incremental outcomes for patients. This, in turn, is forcing pharma companies to reduce costs and development cycle times, while broadening their portfolios to include specialty products, large and small molecule drugs, biosimilars, generics and combination drug/device products.

Pharma companies employ different models to succeed in this demanding new environment. One common challenge across these models — discovery, development and launch of new products — is management of product and process data. As companies "lean out" and speed up their development processes with new technologies, they face increasing challenges with capturing and efficiently managing data as it flows from their labs to their plants around the globe. This is further complicated as companies leverage external development and

CMC	Supply Chain	Quality	Manufacturing	Clinical	Regulatory	Safety	Commercial
Bill of Material	Transportation condition	Management review data — trends on CAPA, product quality parameters	Manufacturing processes	Dosage data	Product registration data	Clinical post-launch AE data	Patient unmet requirements
Unit Operations/Processes	SKU data	Product disposition parameters	Batch record	Regimen data	Labeling	Risk management plans & REMS	Product requirements based on competitor info
Specifications	Planning Bill of Material	Product performance	Equipment requirements	PK/PD data	Commitments	Safety signals/ proportional	
PFD/PTD	Item data	Change control					
Formulation							

Figure 1. Representative Core Drug Product and Process Data across Functions

manufacturing partnerships for speed and cost and they face the same challenges outside the "four walls" of their process and technology landscape. To address this product and process data challenge, pharma companies are beginning to tap into the capabilities of Product Lifecycle Management (PLM) processes and tools. So, for Dr. Smith, a solution is starting to emerge.

SPECIFIC PRODUCT CORE DATA CHALLENGES

Product and process data define a compound, as the compound moves from discovery through development and, hopefully, onto the market. Today, product and process data is created and managed by multiple functions via independent processes throughout the drug development lifecycle (from discovery through to launch). In most pharma companies, information is mostly stored in documents and usually separated among functions. Some companies have dozens of separate databases and/or systems to collect vast amounts of data. As a result, valuable time is lost in collating information that is required to file with regulatory agencies, respond to regulatory questions/investigations, or revisit a technical or management decision. With the above pressures on reducing time to market while improving development and manufacturing efficiency, an accurate and integrated product and process data structure becomes essential. And the existing manual and resource-intensive approaches will not be tolerated.

Based on our work with top pharma companies, we have identified several common challenges with product and process data management. While the ones listed below are more prevalent in chemistry, manufacturing and controls function, there are other product and process data related challenges within clinical, regulatory, quality, manufacturing, supply chain, safety and commercial. Some of the key CMC challenges include:

- **Inadequate linkage between product-related data and their sources slows down product development and tech transfer** — Often, there are "multiple sources of truth" and information is manually entered and then re-entered into downstream systems. For example, critical product information captured in electronic laboratory notebooks (eLNs) is used to draft technical reports that are stored in document management systems. Specific technical reports (and sometimes raw data) are then retrieved and manually assembled for decision-making in a collaboration tool. Finally, the approved information is reformatted into a larger document such as one for technology transfer, where it is then manually re-keyed into manufacturing or supply chain systems. These manual processes not only involve multiple rounds of wasted time on clerical work, but they are also prone to errors that can ultimately prove detrimental to the product in terms of time-to-market or approved label.
- **Document-centric approach detracts from the ability to support timely regulatory submissions and the re-use of information across products** — Typically, key product information is buried in documents and it is difficult to access, maintain and re-use. In addition to the challenges of data re-entry, a document-centric approach prevents teams from re-using the cumulative knowledge across products or technology platforms. We have even seen cases where experiments had to be re-run years later, simply due to the company's inability to find the original set of results.
- **Lack of integrated workflow execution forces the organization to rely on fleeting "tribal" knowledge** — Often, changes to one set of critical product data are not systematically reviewed, approved and communicated to all parties involved. For example, a change in the toxicology profile of a common excipient can impact multiple products and their specifications or impurity profiles, but critical information communicated via e-mail regarding a single material

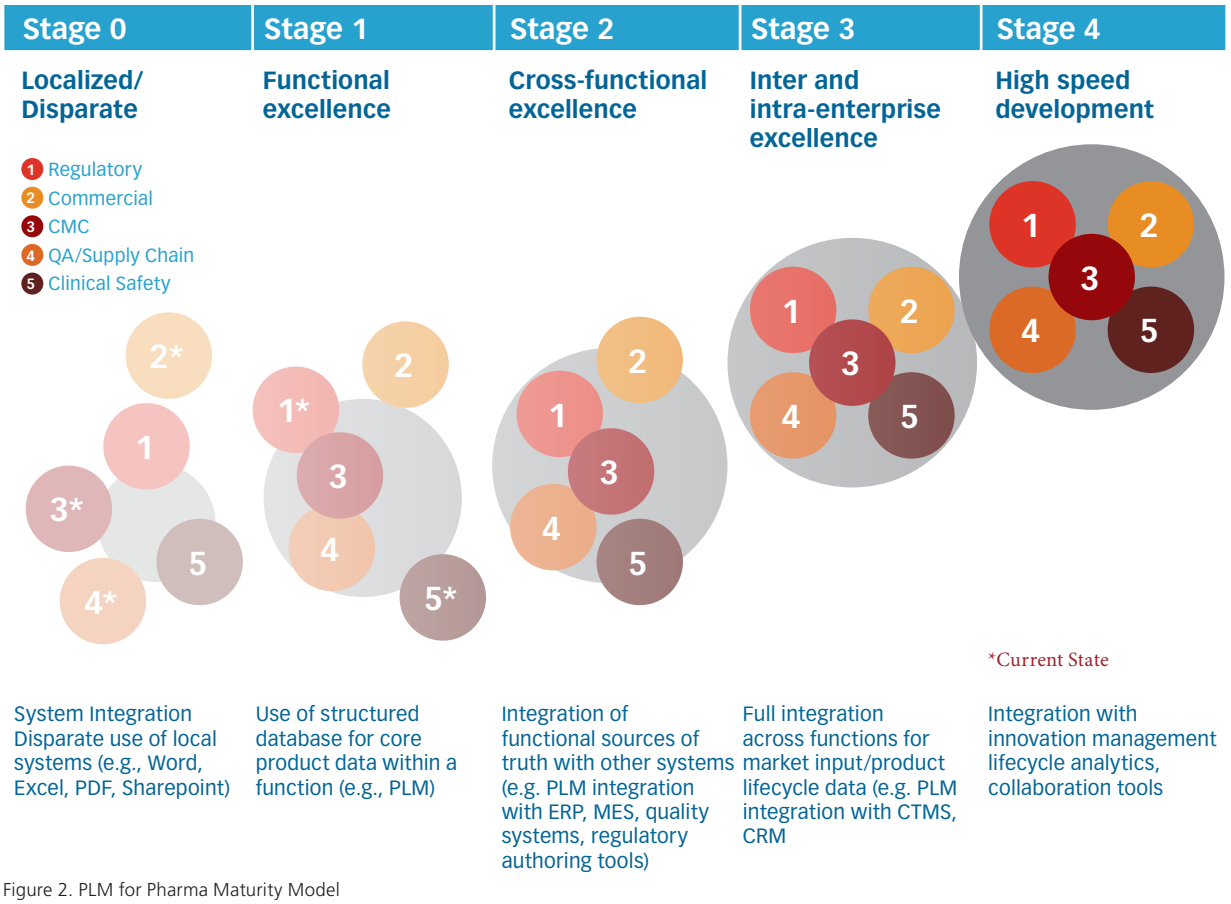


Figure 2. PLM for Pharma Maturity Model

or product is often not leveraged across the portfolio. And, even if it is, this is driven by key individuals and not systematic within the company.

- **Poor project visibility limits the ability to make rapid program decisions —** Data availability is inadequate to make program decisions quickly, as information about project status is locked in function-specific documents and can differ based on system or site. Project tasks and deliverables are manually tracked — with no clear linkage between a task, its deliverable(s) and the corresponding product structure — and require manual update for status and completion.
- **Labor intensive internal and external collaboration prevents bidirectional innovation —** Exchange of information with third party organizations also often happens via emails. This information typically requires additional steps to import, store and manage. As a result, the focus is on management of isolated documents and information and not on the collaborative review and evaluation of that information, for product and process improvements, or effective response to events.

THE RISE OF PLM IN PHARMA

To address these challenges, pharma companies are looking at a variety of solutions. These include enhanced semantic search capabilities, utilization of collaboration tools and more rigorous approaches to Master Data Management. But one of the more intriguing options emerging is to adopt and modify PLM practices that have proven successful in other industries.

PLM is the business capability of leveraging product data throughout a product's lifecycle in order to gain efficiency from a single source of accurate, complete and timely product-focused data. Modern PLM is critical — and widely adopted — in the electronics, automobile and aerospace/defense industries. More recently, it has also become prevalent in food/beverage, consumer packaged goods and the medical devices industries. Key benefits include:

- Use of data across products, to improve time to market and support portfolio analytics
- Ability to manage product information (structure, requirements, project plans, changes) along the end-to-end product lifecycle, across core commercialization functions

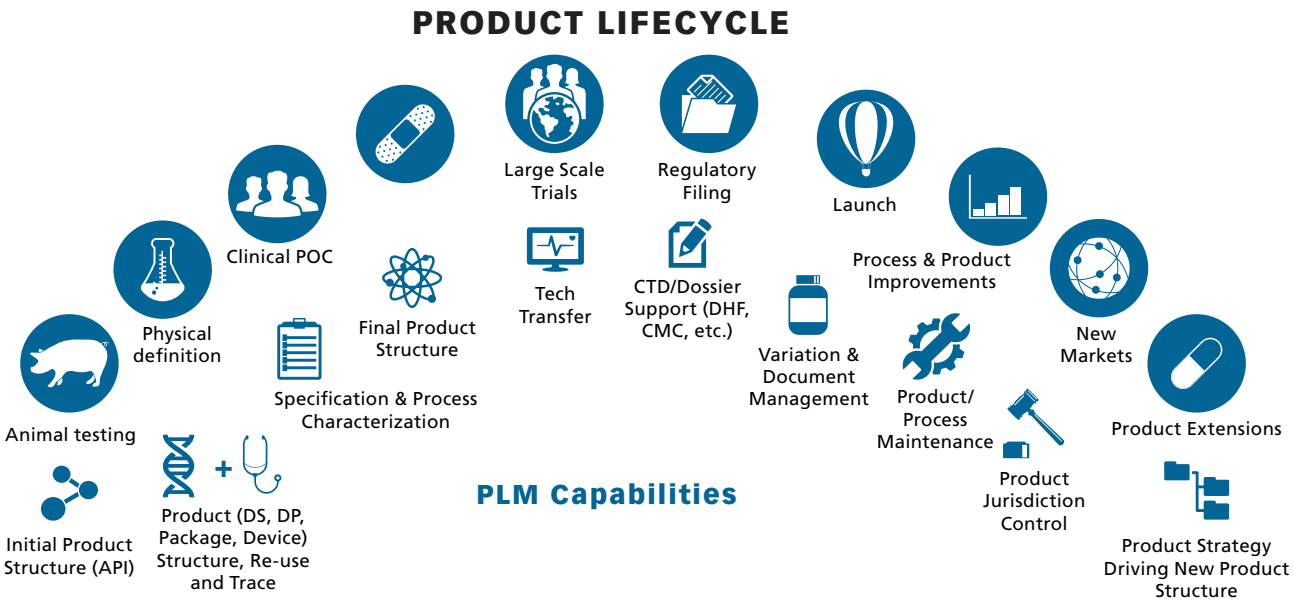


Figure 3. Vision of a Mature Stage 2 PLM Maturity in a Pharma Company

- A secure collaboration platform for internal and external co-development, review of changes and resolution of adverse events or deviations
- Automation of administrative tasks, enabling scientists and technical experts to focus on their core roles instead of data search, information retrieval, or document writing
- Re-use of existing data for product variation management to further accelerate time to market

To begin to understand the value of PLM in pharma, companies have started by asking a critical question: what are the core drug product and process data in a pharma setting? While companies are tackling this question from various functional perspectives, we believe that core drug product and process data is truly cross-functional in nature — and must be created and consumed across multiple functions including clinical, CMC, regulatory, quality, manufacturing, supply chain, safety and commercial. Figure 1 depicts some of the representative core drug product and process data created, maintained and consumed by these functions.

How are core drug product and process data handled by these various functions? While some pre-commercial functions such as clinical have more experience managing data to comply with Good Clinical Practices

PHARMA COMPANIES ARE TURNING TO PLM TO ADDRESS CHALLENGES, BUT THEY SHOULD BE THOUGHTFUL ABOUT ITS DESIGN AND IMPLEMENTATION.

(GCP), other functions do not. Furthermore, each function has tended to advance its product and process data management capabilities independently to serve their own purposes, as they transfer documents and data during development and technical transfer to commercial operations. We refer to this progression of product and process data management capabilities as the "PLM for Pharma Maturity Model," as depicted in figure 2.

Stage 0 depicts immature product and process data management where product information is captured in documents, without a standard format and stored in local systems. The information sharing across functions is highly manual, and scientists or managers waste a lot of time looking for information, creating reports and often copying data from one place to another. This is largely the status-quo of product and process data management in the pharma industry, in functions such as CMC, quality and supply chain.

On the other hand, some functions are more advanced in their data management capabilities today, driven by the absolute need to capture, re-use and correlate product data. An example is the clinical function, where fairly mature structured databases (e.g., Electronic Data Capture (EDC) and Clinical Trial Management System (CTMS)) are in place to consistently capture data in a standard format. This enables easy search and analysis of large sets of data. We see some pharma companies leveraging functionally focused capabilities to advance to the next stage of maturity, Stage 1. In this stage, we see standardization of data structures, transition from document-centric to data-centric models and consolidation of data into one single source of truth, albeit in one or a few functions. These outcomes can be enabled by traditional PLM solutions.

However, drugs cannot be developed and manufactured in a siloed manner. Functions must share data in an integrated manner in order to efficiently progress through the development, launch and commercial product lifecycle. This need brings us to Stage 2 of PLM for pharma maturity. A typical integration point for sharing of core product and process data occurs between PLM (e.g., CMC-derived data), Manufacturing Execution System (MES) (e.g., manufacturing process data) and Enterprise Resource Planning (ERP) (e.g., supply chain-related data). This integration facilitates a smooth tech transfer and can accurately track product disposition. Another example includes the integration of core product and process data derived from CMC with regulatory information management systems, so that the burden of creating and validating regulatory submission documents can be reduced. Figure 2 represents one pharma company's vision of a mature Stage 2 PLM model (with plans to achieve it during the next 3 years).

Stage 3 of maturity is achieved when product and process data management is integrated across all the internal development and commercialization functions and with external partners. This is where marketing data or competitive information can inform the target product profiles in real-time and product development can become more adaptive and flexible. Tight integration across functions also allows creation of the full Common Technical Document (CTD) or similar dossier submissions, including potential vendor participation and ultimately accelerates the timeline to filing. Data Lake and semantic technologies are tools that can enable the full integration.

Finally, Stage 4 represents the future of PLM for pharma, where historical and real-time information, including non-conforming data and hypothesis across functions, are synthesized to inform adaptive and predictive design of a product. This typically involves advanced collaboration, analytical and cognitive tools across the integrated and logical data flow to achieve high-speed product development throughput. This stage is still aspirational for most pharma companies, but is effectively used by leading companies outside of our industry.

PLM CAN MAKE A DIFFERENCE

As the pharma industry strives to achieve increasing efficiency in response to global economic challenges, new capabilities such as product and process data management, collaboration and analytics are needed. Some leading technology providers are tooling their traditional PLM solutions — broadly used in other industries — to meet pharma's needs, the specific requirements of integrating product and process data. Pharma companies should think strategically about the best ways to adopt these capabilities, carefully select the most appropriate solutions and then design creative deployments to make a set of solutions co-exist across various functions. Increasingly, pharma companies are turning to PLM to address these challenges, but they should be thoughtful about its design and implementation, as the "right" architecture for pharma may look familiar in places but very different in others, when compared to other industries.

Next-Generation Innovation

Streamlined strategies secure pharma's future as the industry thinks outside the pill box

By Karen Langhauser, Chief Content Director

AS DRUG PRICING REACHES what some might argue is the height of public and political scrutiny (thanks Martin Shkreli), consumer expectations rise, and the blockbuster model continues its well-documented demise, the market has made innovation mandatory for the pharmaceutical industry. Bottom-lining it, PricewaterhouseCoopers stated in its "Managing Innovation in Pharma" report, "the rewards for success are high and the risks of failure can threaten a company's very survival."

To say that the pharmaceutical industry lacks innovative ideas would be doing a tremendous disservice to an industry that has sustained decades of respectable growth along with a healthy list of historic medical achievements. More recently, the last five years of Thomson Reuters Top 100 Global Innovators lists consistently report pharma as one of the largest industry sectors represented.

Rather than isolated examples of innovation in the form of single new molecules, today's market calls for next-generation innovation in the form of innovation strategy.

For many drug manufacturers, innovation strategy involves streamlining an increasingly complex manufacturing system. This type of next-generation innovation wades through the growing sea of new ideas and emerges with the strategies that deliver a clear, focused value. How does this play out in pharma in 2016? In the form of targeted acquisitions and partnerships, personalized treatments, efficient outsourcing partners and properly integrated technologies.

Delivering authentic innovation in today's pharmaceutical environment is a momentously complex task with one very succinct emphasis. That emphasis, according to Dr. Clive Meanwell, CEO at The Medicines Company and recent recipient of the 2016 Dr. Sol J. Barer Award for Vision, Innovation and Leadership, is a "sharp focus on what customers really need."

MERGERS, ACQUISITIONS AND PARTNERSHIPS

PwC's Health Research Institute's annual report predicts that 2016 will be the "year of merger mania" in healthcare, specifically mentioning the pharmaceutical and life sciences sector. According to the report, "drug companies are looking beyond traditional M&A by acquiring 'beyond-the-pill' products and services to bolster their portfolios and pipelines of drugs."

Consolidation has typically been a dirty word in pharma and rarely appears in the same sentence as innovation. But a handful of forward-thinking companies are recognizing the need to innovate beyond merely acquiring new molecule formulations. Dwindling (though definitely not gone) are the days when pharmaceutical companies would hunt for deals to boost up specific therapeutic areas, aiming to completely dominate that space. Under immense pressure to optimize performance, today's companies are taking a heavy look at the systems and services behind these new drugs and making strategic acquisitions with an eye toward innovative services and digital technology.

Teva Pharmaceutical made a strong move in the digital space in September with its purchase of smart inhaler company, Gecko Health. Prior to that acquisition, Teva, in collaboration with Phillips Healthcare, launched

Sanara Ventures in Israel. The collaboration will invest approximately $26 million to support 40-50 early-stage digital healthcare and medical device companies in the next eight years.

The last few years have seen numerous innovative crossovers as pharma looks toward unconventional partnerships, specifically in the tech field. In 2014, Google's R&D business, Calico, partnered with AbbVie to focus on age-related diseases. Around the same time, Google X Labs teamed with Novartis to develop glucose monitoring, smart contact lenses and early last year, partnered with Biogen to explore wearables technology in multiple sclerosis.

But M&A is not always about innovation. Sometimes it's about money — often in the form of tax inversion deals. The $160 billion dollar 2015 Pfizer-Allergan merger created the world's biggest drug company — and will move Pfizer's domicile from the U.S. to Ireland, dropping its corporate tax rate by about 7-8% percent. Pfizer is not alone in capitalizing on this tactic. In 2014, Mylan acquired Abbott Labs and moved its headquarters to the Netherlands. In 2014, AbbVie reconsidered its $54 billion acquisition of Shire — a deal that would have allowed AbbVie to reincorporate in Britain — after the Treasury Department announced new rules taking aim at inversion deals. According to a Bloomberg report, about 51 U.S. companies have reincorporated in low-tax countries since 1982, including 20 since 2012.

TARGETED OUTSOURCING PARTNERS

As their goal is to serve the unmet needs of the pharmaceutical and biotech industries, contract manufacturing movements are often reflective of the drug industry demands. Like the industries it serves, the contract services market has not been immune to consolidation. In fact, according to Visiongain's "Pharmaceutical Contract Manufacturing World Industry and Market Outlook 2015-2025," about 30 CMOs account for more than half of the industry's revenues and, in the last three years, there have been 18 acquisitions in the CMO space.

Despite a reduction in supplier options, pharmaceutical manufacturers are becoming smarter and more specific when it comes to choosing contract manufacturing partners, expecting a higher degree of flexibility.

According to Peter Soelkner, managing director at Vetter Pharma, "drug companies are making every effort to reduce and simplify their network of different service providers. What they want to achieve, whenever possible, is a solution that equates to 'one-stop-shopping.' They expect that any partner they choose to work with must be strategic in their efforts, not simply tactical."

Vetter is in the process of multiple facility expansions and technology upgrades, including the implementation of an internally engineered restricted access barrier system (RABS) concept for increased operational excellence in aseptic manufacturing. The RABS technology allows for faster start-up time, ease of changeover and reduced capital costs.

As pharmaceutical companies ramp up investment in flexible in-house technologies and continue acquiring their own contract services providers, contract manufacturers are understanding the need to specialize — especially surrounding the growth of biologic drugs and biosimilars, including the growing demand for novel therapies. CMOs are increasing their investments in single-use technologies for biopharmaceutical manufacturing and continuous manufacturing processes.

Aware of their critical role in an increasingly sophisticated global supply chain, today's contract manufacturers are innovating to provide high quality, flexible production.

INTEGRATING TECHNOLOGY

Trends and advancements in the pharmaceutical industry tend to trigger cascading responses from linked industries, such as equipment, packaging and drug delivery devices. Take, for example, the continued focus on patience compliance and biologics, which has evolved into a growing market for combination products — the marriage of biological products, drug containers and drug delivery devices.

Drug manufacturers who have typically only dealt with making drugs have needed to broaden their in-house expertise or contract manufacturing reach to be able to address the technical, commercial and regulatory issues that have emerged with combination devices.

According to Jessica Buday, senior manager, Process & Operational Excellence, Ferring Pharmaceuticals, the pharmaceutical landscape today involves, "being prepared for not just the new products, but the new technology that is required (preferably in-house) to manufacture them. For instance, drug delivery now involves more than just tablets and vials — there is the entire world of combination devices. The companies that master development and validation of these devices will put themselves at the forefront. In manufacturing, that includes making sure we have the equipment for commercializing these devices."

Ferring Pharmaceuticals, known for its reproductive health treatments, also focuses on offering more effective drug-delivery devices, including needle-free devices and transdermal delivery technologies. In March of last year, Ferring entered the U.S. pediatric endocrinology market with the acquisition of Zomacton growth hormone deficiency treatment and with it, the Zoma-Jet needle-free delivery device from Teva Pharmaceutical.

For West Pharmaceutical Services, a company at the forefront of combination devices, successful drug therapy is a comprehensive strategy. "Our customers work hard to come up with innovative new molecules, but a drug molecule is completely useless unless delivered to patients in the best way," says Graham Reynolds, vice president and general manager, Biologics, West Pharmaceutical Services. For West, there are four elements that need to be considered in successful drug therapy: the molecule itself, the container that holds it, the delivery system that administers it and the fourth — often forgotten element — patience adherence. "The interfaces between these elements are as critical as the phases themselves," adds Reynolds.

These "interfaces" are also driving equipment trends. For example, the increasingly important role that aseptic processing single-use systems play in the fill/finish process. Single-use components are helping manufacturers decrease time spent on cleaning and validation, thus saving them money. The newer, disposable technology enables fully integrated, continuous production.

It's not so much the stand-alone technologies that drugmakers are reaching for, but rather, targeted innovation that enhances overall the effectiveness of the process.

PRECISION MEDICINE

Precision medicine, as defined generally by the National Institutes of Health, is an "emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment and lifestyle for each person." While still in somewhat of a nascent stage, public interest has grown since last January when President Obama announced the Precision Medicine Initiative (PMI) in his State of the Union address.

As the pharmaceutical industry moves forward with its quest to innovate and streamline, this patient-centered, data-driven approach makes sense. Brad Campbell, president and COO of Amicus Therapeutics, points to the rise of precision medicines as a real example of innovation. Precision medicine, according to Campbell, enables us to "drive science toward not just a specific disease but a specific genetic substrate. It helps improve the risk-benefit ratio, removing 'waste' from the system."

Amicus is in the process of seeking global approvals for its lead product candidate, migalastat, a personalized medicine in late-stage development to treat individuals with Fabry disease. Fabry disease is a rare, inherited disorder caused by deficiency of an enzyme called α-galactosidase. In terms of Amicus' work on its migalastat treatment, this precision medicine approach is designed for patients with "amenable mutations," that is, specific mutations that are capable of responding to oral migalastat as a monotherapy treatment. Amicus' extensive preclinical and clinical work has characterized the properties of nearly 800 known Fabry disease-associated mutations in an effort determine which patients are most eligible for treatment.

The result? "The use of elegant science to identify, with high precision, which patients will benefit," states Campbell.

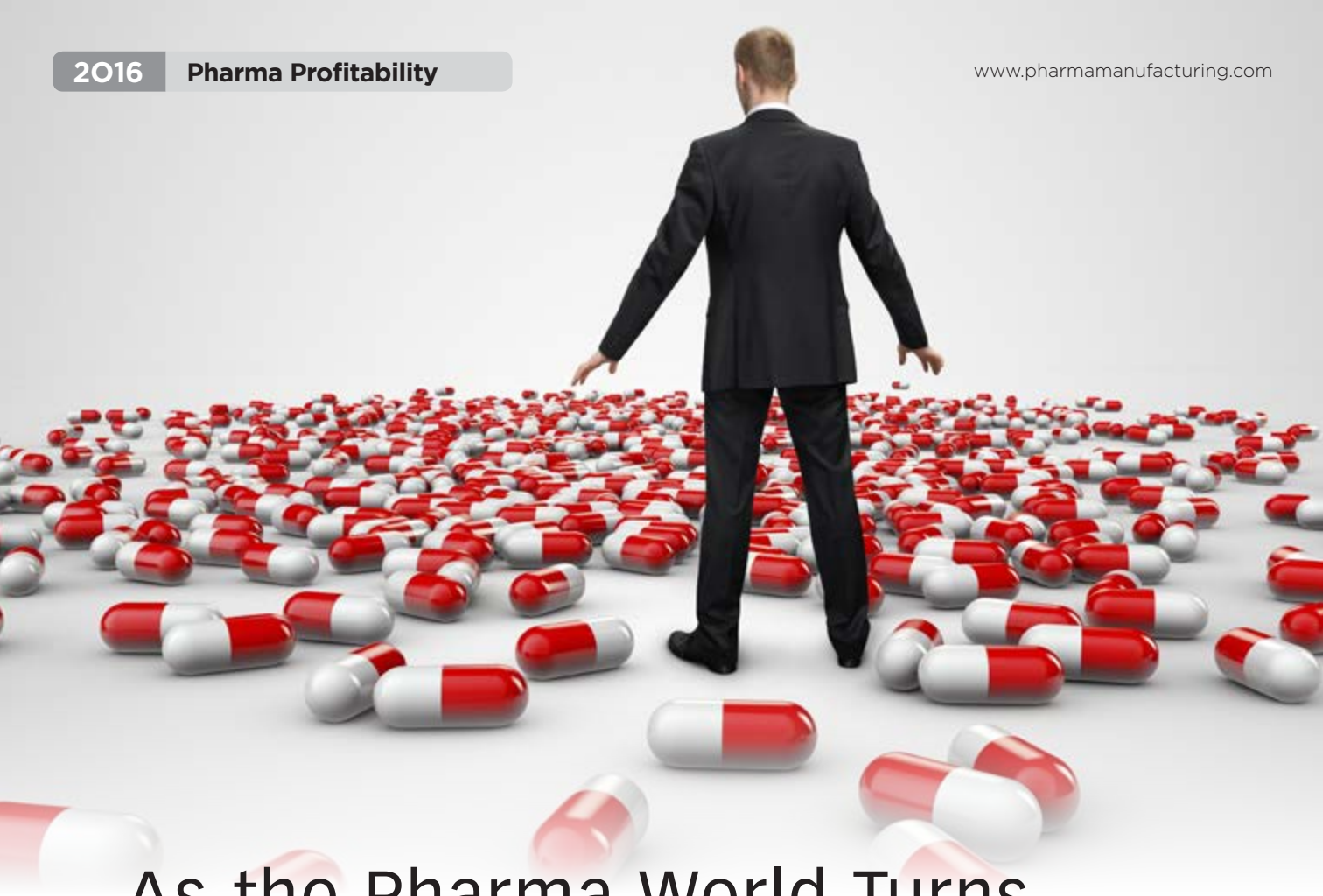
In June 2015, the National Cancer Institute (NCI) announced a precision medicine trial touted as "the first study in oncology that incorporates all of the tenets of precision medicine." The trial, called NCI-MATCH, seeks to determine whether targeted therapies for people whose tumors have specific gene mutations will be effective, regardless of their cancer type. Obama's PMI budget request included $70 million for NCI to scale up efforts to identify genomic drivers in cancer. The robust list of pharmaceutical partners involved in NCI-MATCH includes Novartis, Pfizer, Boehringer Ingelheim, AstraZeneca, as well as device manufacturer, Thermo Fisher Scientific.

NEXT GENERATION DEMANDS

Specifically speaking about precision medicine, Campbell stressed the industry's need to "move away from the shotgun approach" to treatment, but perhaps this statement has wider implications for today's pharmaceutical industry. The practice of cranking out rapid-fire innovation in the form of new molecules with the hopes of finding the next blockbuster is being replaced by targeted innovation strategies that demonstrate actual patient value and can be duplicated across an enterprise.

Today's patients are more informed and connected with their health decisions than ever before. With that in mind, pharmaceutical manufacturers are making smarter choices when it comes to acquisitions, new technology and contract partners. Next-generation patients demand next-generation innovation, and the pharmaceutical industry is rising to the challenge.

Editor's note: Special thanks to our friends at Choose New Jersey and BioNJ for their assistance in the form of sharing their vast network of innovative contacts with us. Please visit them at www.choosenj.com and www.bionj.org.



As the Pharma World Turns

Pharmaceutical Manufacturing's readers continue to find career satisfaction despite the industry's day-to-day drama

By Steven E. Kuehn, Contributing Editor

A CAREER in pharma is no soap opera, but it can often feel like one. Managing a career, especially one that often requires advanced degrees and intensive and sustained professional focus, is tough enough without the added drama of the ups and downs of the commercial marketplace. And so it goes for many working on the pharmaceutical industry stage who are toiling diligently to meet their employer's business goals as well as their own career aspirations. Each year since the magazine began publishing in 2002, *Pharmaceutical Manufacturing* has surveyed its readership to gain a sense of how folks are doing career-wise, as well as to get an idea of how their attitude reflects current and future trends.

Response to this year's study was relatively strong with 268 completing surveys and 240 readers offering a response to every one of the questions (because readers were not required to answer each question).

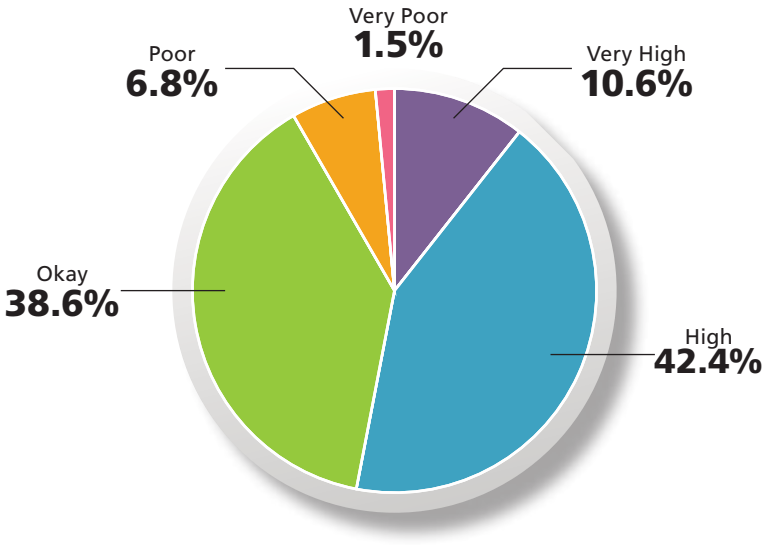
MARKET EFFECTS

There should be little doubt that pharma is moving in some new and interesting directions. While there is no need to recite the industry's current catechism of looming patent cliffs, diminished blockbuster opportunities and more direct regulatory oversight of manufacturing operations, pharma and life science companies are reacting to market forces in a variety of familiar ways. Chief among them is the way companies, by necessity, are arranging themselves to be competitive and successful. Asked "How have market and competitive forces affected your company recently?" 43.5 percent chose "Major business unit or operations restructuring." The response, similar to last year, points to a dynamic that has the ability to either kill or launch one's career in pharma. Mergers or acquisitions came in second place at 36.6 percent, which is not surprising; in 2015, some of the largest M&A deals were in the pharmaceutical sector. According to analysts at PwC, "transformational deals" (transactions valued at $10 billion and above) accounted for 58 percent of total deal value in the first half of the year. Huge pharmaceuti-

cal "megadeals" including AbbVie's $21 billion deal for Pharmacyclis and Pfizer's $17 billion deal for Hospira, garnered 17 percent of total M&A deal value — some $150 billion says Forbes Magazine — for the first five months of 2015.

These upheavals can cause a lot of angst among employees. In a flip from last year, 52.5 percent (as opposed to 48 percent in 2015) indicated they were more concerned with job security than last year. What are they concerned with? Top of mind for most (55.5 percent) was the fear that internal cost-cutting (often the familiar outcome of mergers and/or acquisitions) may soon have a negative impact on their careers. Others (25.6 percent) identified "External financial pressure on my company due to expiring patents or circumstances surrounding failed product development or regulatory approval." Again, business circumstances and other events that trigger organizational moves to manage costs, trim redundant functions, lop off idle capacity, etc., have always been identified as a job security pain point for PhM's readers. Here's one reader's appraisal: "I was satisfied with the variety and the assignments — when it was held by a major company. My site was independently run but was still overall controlled by a larger company. Pay was adequate, even though the work was hard and there was a lot of it! Job security was assured. Opportunities for growth were great — afraid things will change drastically under new ownership!"

Figure 1. Please rate your overall level of job satisfaction.



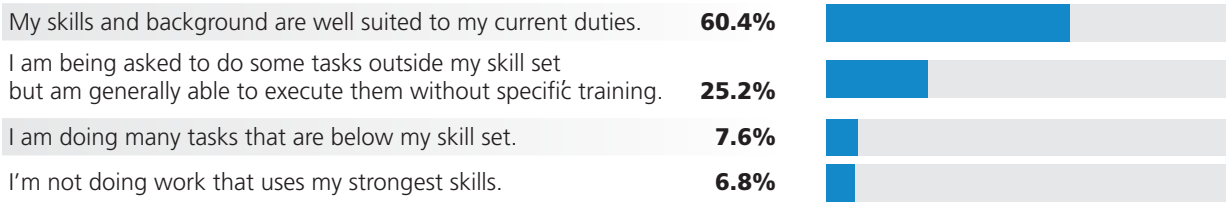
Through their answers, we gather a pretty clear picture of the demographic profile of those responding. Not surprisingly, respondents are mostly male; gender was split in their favor 80 to 20 percent (of 240 total responding) and maturing, with some 42.7 percent 55 older, followed by those 40-54 holding down the fort. Yes, there are younger professionals out there, but at 2.9 percent for 20-29 year-olds and 13.8 percent for 30-39 year-olds, it's clear that the industry is graying. PhM's readers are by most measures pretty smart. Nearly 20 percent of those responding indicated they have a Doctorate, another 23 percent a Masters in something other than Business, and most remaining (38.6) possessing a Bachelor's degree. We did catch a few responses from those in the trades and those (perhaps) working the line with high-school degrees. Of those with degrees, most have either a Chemical Engineering, Pharmaceutics or Chemistry degree, with the rest possessing Business, Electrical Engineering, Mechanical Engineering, Bio Chemistry and similar technical or science-oriented educational backgrounds.

One of the great things about PhM's 2016 Reader Survey is that we tap into the ethos of operational types. This year, most (70.9 percent) fill operational roles (sum of operational categories) with nearly

Figure 2. What were the biggest challenges you had to face in the past year?

New product(s) introduction.	**30.8%**
Plant or business unit expansion.	**24.2%**
Increased workload due to organizational changes.	**58.1%**
Lean, Six Sigma or other Operational Excellence initiatives.	**16.2%**
New role or position internally.	**21.9%**

Figure 3. How would you rate the suitability of your skills to manage current responsibilities?



a quarter (23.2 percent) specifying involvement in quality assessment and quality control, and 17.4 percent identifying themselves with manufacturing operations. Research and development types were represented as well, with 16.6 percent. In single digits are the rest, with PhM readers working in plant engineering and design, IT and facility management to round out the occupational orientation of those responding. Regardless, PhM is reaching the veterans, with 49 percent indicating they've been in the industry more than 20 years. The next largest group (30.7 percent) have 11-20 years experience, with the remainder ranging from one to ten years running their "lines" on the pharma stage.

Responding readers represent the diversity in pharma — parsed rather evenly across the industry's major segments, responding readers come from all sectors including Contract Manufacturing, traditional "Big" Pharma, Generic Pharma, Bio Pharma and small or midsized specialty pharmaceutical manufacturers. Regardless, compensation is healthy and reflects the seniority and experience of PhM's readers. For example, 30.8 percent have salaries between $100 and $150K, with next largest group (15.8 percent) making $150 to $200K annually. In third place were those making between $80 and $100K (13.8 percent). Some "A" list actors (9.6 percent) indicated their salary was above $200K, and in this industry, it's likely they earn it. Did folks get raises last year? Most got at least a 3 to 5 percent bump. With the average annual salary boost hovering around 4 percent, those indicating higher raises (a few indicated their raises were above 16 percent) reveal the industry's healthy compensation and retention environment.

MORE MONEY, MORE HAPPINESS?

It's been said a million times that money can't buy happiness, but it can buy you things that make you happy. Most all responding measured their "satisfaction" as positive. Those rating it "High" were legion, with 42.4 percent indicating they were pretty happy with their jobs all things considered. Some, apparently, are ecstatic ("Very high" 10.6 percent). A big chunk, 38.6 percent, indicate that satisfaction was "Okay" which for most people is reality and (again) all things considered, a decent place to be attitude-wise; especially in pharma. Fortunately, those feeling not-so-great about things and rating satisfaction as "Low" or "Very low" were only about 9 percent of total respondents.

As mentioned, there is a bit of angst out there concerning job security. Market forces are adding to the burn and readers identified a number of events that trigger concern. More outsourcing, plant closings and similar events are making their mark, good and bad, on people's careers. What are the keys to pharma employee satisfaction? In the middle of the pack were "Opportunities for Advancement," "Salary and Benefits," and "Job Security" garnering 17.4, 17.8 and 14 percent (respectively) of our respondent's choices. What is really interesting is that most of PhM's responders (32.6) indicate "Challenging Work" brings them the most satisfaction. Here's how one of PhM's readers articulated it: "My new position offers me a blank canvas on which to lay out and execute my vision for various new initiatives. It is challenging mostly because I have never done much of what I intend to do, but I am finding that my

Figure 4. Does your company offer access to a formalized program of training to support business or operational excellence goals?

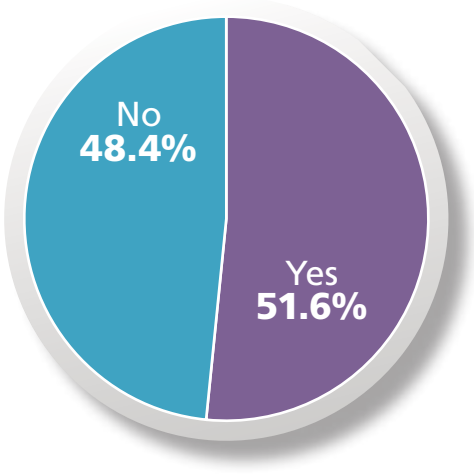
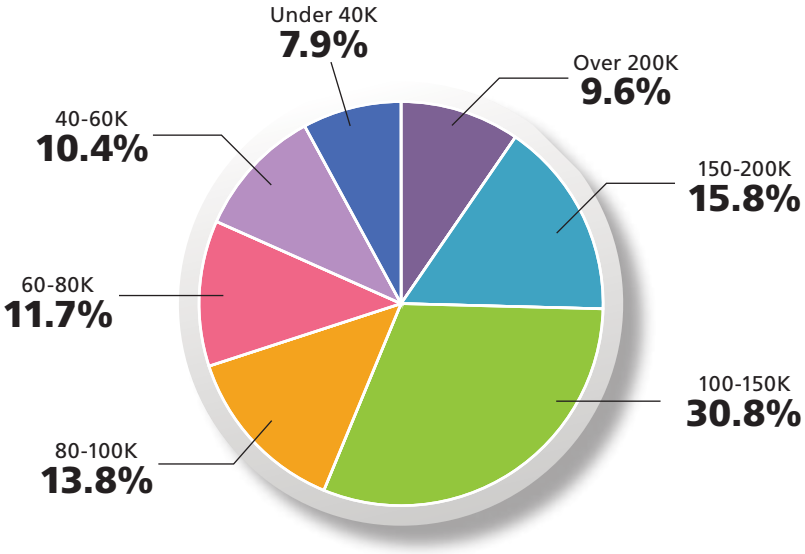


Figure 5. What is your current annual gross salary?



colleagues are a huge and helpful resource. I also do not have constant micromanagement, which has allowed my creativity to flourish."

So, what were some of those challenges? Again, restructuring and M&A activity set the stage. We asked readers what were their biggest challenges. Overwhelmingly, 58.1 percent cited "Increased workload due to organizational change," winning the People's Choice Award when it comes a career in pharma. Others were challenged by "New product introductions" (30.8 percent), "Plant or business expansion" (24.2 percent) and 21.9 percent indicating a "New role or position internally" got people's hearts racing.

STAYING RELEVANT

For any professional in pharma, the biggest challenge career-wise is staying relevant, with skills and experience that are valued by colleagues and employers, over the span of one's career. New systems, new processes, new products … new … whatever, will always be a part of one's pharma career. Keeping pace with industry change is a paramount priority. How do PhM's readers feel? Most are confident that they are up to the challenge; "How would you rate the suitability of your skills to manage current responsibilities?" 60.4 percent indicated, "My skills and background are well suited to my current duties." The responses to the question also indicated some of the resilience and flexibility one needs to stay relevant — "I am being asked to do some tasks outside my skill set, but am generally able to execute them without specific training," 25.2 percent of respondents offered that resolute assessment.

Are companies supporting continued relevance and competence with training? According to responses, half said their companies offered formal training and the other half said they did not. For those employed by companies that do offer formalized training we asked for comments. They ranged from cynical to superlative, but one stood out: "The majority of staff that participate in these training programs have a lot of free time, and are not very experienced. When they complete the training, they are credited as experts, though they know only a few things; the training is not at all comprehensive, yet they are treated like they know more than others. It's a Dilbert comic strip that isn't funny..." Just another indicator that in a large, corporate environment good intentions and resources do not necessarily translate into effective workforce development tools.

THE SHOW MUST GO ON

It's clear from this year's study that the actors on the pharma stage are, by-in-large, satisfied with their careers, relatively happy with their organizations and confident their skills and abilities will keep them relevant and valuable to their employers. Although money is a big part of overall career satisfaction, most of PhM's responding readers find the industry's challenges as a primary driver of career satisfaction. Bravo!