

CASE STUDY

PharmaPendium®

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Regulatory Pathways



SUMMARY

PharmaPendium provides Regulatory Affairs professionals with robust high quality information that supports drug approval processes and decisions with instant access to current and archived approvals, drug reviews, preclinical and clinical comparative data and regulatory context.

One valuable source of a drug's entire history of development, pre-clinical testing, regulatory review and approval is PharmaPendium.



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ABSTRACT / SUMMARY

In an environment of change within the Pharmaceutical Industry, the role of Regulatory Affairs has never been more central to the success of an organization. Recent trends towards innovation, improvement and extension of previously approved products and the manufacture of generic medicines mean that an appreciation of the regulatory pathways available to the regulatory professional is vital to the role. Regulatory hurdles are numerous, especially in terms of the requirements for scientific data, regulatory information and local regulatory intelligence. One valuable source of a drug's entire history of development, pre-clinical testing, regulatory review and approval is PharmaPendium® which provides an unmatched opportunity to strengthen regulatory submissions and accelerate approval timelines.

Regulatory Environment

Perhaps more than ever before in its long and varied history, the Pharmaceutical industry is experiencing a period of change and challenge. In this arena of innovation and increased regulation, the role of the Regulatory Affairs professional becomes steadily more integral to the drug development process.

With much discussion revolving around the peak of the "patent cliff", 4 of the top 10 once biggest blockbuster products will experience patent expiry during 2012 alone. With the resultant loss of revenue (estimated to be approximately \$140 billion annually) largely failing to be off-set by new product pipelines and approvals over the coming few years, pharmaceutical companies must evolve and innovate.

Such innovation has led to a number of clear trends developing over the past few years. In the short term, line extension, reformulation, novel drug delivery mechanisms and addition of new therapeutic indications for existing products have all proven to be successful strategies for preserving patents and revenue streams. In the longer term, the industry is demonstrating a distinct trend towards the development of technologically innovative biological, vaccine and orphan products and perhaps ultimately advanced therapies such as cell and gene therapy. Other forms of revenue maximisation come in the form of the penetration of emerging Markets, over the counter (OTC)-switching and an increased interest in Generics by previously innovator-only companies.

This movement towards innovation comes amidst the backdrop of a steadily changing regulatory and health technology environment. Faced with the challenges of counterfeit medicines and evertightening requirements for Quality, Safety and Efficacy, the regulatory environment has arguably never been so challenging. As a result, the role that Regulatory Affairs departments play in the future success of their organisations has never been so pivotal.

“The Regulatory Environment is always changing and always challenging. Increasingly, we are seen as the department that makes things happen.”

– R.B. (Large Multinational Pharmaceutical Company)

Historically, Regulatory Affairs may have often been portrayed as the group whose sole remit was to prevent other departments doing what they wanted to do. However, this outdated impression has gradually been replaced (within many organisations, at least) with the view that Regulatory professionals are facilitators. Through external interactions with Regulatory Agencies, and internal interactions with clinical research, marketing, labeling and artwork departments, legal teams, drug safety and pharmacovigilance units, manufacturing or quality groups and business strategy/commercial departments, the Regulatory Affairs professional is central to the achievement of any organization’s future milestones.

Regulatory Pathways

With the dual factors of increased regulatory pressure and diminished product pipelines working in parallel, it is no surprise that a clear downwards trend has been seen in the number of new medicines being successfully brought to market. Indeed, between the years 2005 to 2010, the total number of US approvals more than halved. This was partially off-set by a decade-high peak of 35 approvals in 2011, although preliminary data for 2012 have shown a significant downturn once again.

Whilst this downward trend is concerning, closer examination of these numbers reveals that in recent times, biotech products have actually been twice as likely to receive FDA approval than more traditional small molecules. The importance of continued innovation within the industry is therefore underlined, both through the development of technologically enhanced products and the effective extension and further development of previously approved products.

The US Regulatory Framework provides for 3 distinct regulatory approval pathways (as outlined in the Food, Drug, and Cosmetics Act (FD&C Act)), allowing for the registration of novel compounds, new drugs containing similar ingredients to previously approved products and generic copies of previously approved products.

The 505(b)(1) NDA pathway applies to the registration of New Drugs only. Due to the large amount of data required to support such applications, novel drugs inevitably require extensive clinical and non-clinical studies in order to demonstrate the Safety and Efficacy. Associated with this data requirement is an inevitable cost in terms of money, resource and time. Market exclusivity granted for approvals via this pathway is 5 years.

“Understanding the Regulatory Pathways available to us can be the difference between success and failure. The correct choice can have a major impact on the timing of product approval and revenue generation.”

– P.C. (Multinational Healthcare Organization)

The 505(b)(2) NDA pathway applies to the registration of a New Drug that contains a similar active ingredient as a previously approved product –in a sense “improved Generics”. The requirement for additional studies is therefore only a fraction of those required via the 505(b)(1) NDA pathway, leading to shortened timelines and reduced cost. Indeed, one can partially rely on the FDA’s previous findings regarding safety and efficacy of a reference product to support one’s own application. Market exclusivity granted for approvals via this pathway is between 3 and 5 years.

The 505(j) ANDA pathway applies to Generic copies of a previously approved innovator product. The application itself is abridged (referencing the clinical and nonclinical studies performed for the approval of the reference product) and only bioavailability/bioequivalence (BA/BE) studies are required. Market exclusivity granted for approvals via this pathway is only 0.5 years.

The three regulatory pathways available through sections 505(b)(1), 505(b)(2) and 505(j) provide three very different options for consideration. However, despite all three pathways being available since 1984, it is only relatively recently that 505(b)(2) applications have been commonplace. Driven by the increasingly challenging drug discovery process, pharmaceutical companies are regularly seen to be exploring innovative ways of generating revenue from already existing products as well as developing innovative new molecules.

Recent data show that approximately twice as many products receive FDA approval via the 505(b)(2) route than the more traditional 505(b)(1) application process, reflecting how organisations are looking to generate new revenue streams and data exclusivity from the relatively short approval timelines that this pathway affords. It is fully anticipated that this trend will continue over the coming years.

The 505(b)(2) drug development pathway is specific to the US Regulatory Framework. However, the overarching themes of depleted product pathways, patent cliffs and the need for continued innovation are truly global. Similar trends are therefore evident within the EU, with dramatically increased numbers of Generic and line extension applications over the past few years and a growing number of innovative biological and orphan products successfully reaching the market.

“The It’s not necessarily what you know – more often than not it is a case of understanding where to get the information from”

– L.A.B. (Global Regulatory Consultancy Agency)

Regulatory Hurdles

Whilst the drug discovery paradigm may be changing as increasingly innovative ways of generating revenue are pursued, the journey from compound to approved drug is lengthy and costly. Whilst overall figures are much argued and discussed, a figure of approximately \$1000-2000 million and a 10-15 year process may not prove untypical. Throughout this process, a cohort of perhaps 10,000 potential compounds might yield 1000 screened candidates of which 100 may be deemed worthy of further development. Of these 100 candidates, 10 may undergo clinical trials of which hopefully a single drug will be identified that is worthy of registration and approval.

The obstacles to regulatory approval are numerous. However, such regulatory hurdles can be successfully and pro-actively navigated with the help of PharmaPendium® (www.pharmapendium.com), an unmatched source of data relating to the entire history of a drug’s development, pre-clinical testing, regulatory review and approval.

This repository of documentation provides a unique opportunity to strengthen regulatory submissions and thereby accelerate approval timelines, providing instant access to all archived FDA Approvals since 1938. Within this repository, more than 1.3 million pages of drug reviews can be found, encompassing more than 3022 unique drug reviews. In addition, crucial comparative data and numerous regulatory precedents provide the opportunity for preempting and avoiding potential issues, further strengthening the case for regulatory approval.

Drug Development and Pre Clinical

Whilst much regulatory activity is concerned with the registration and maintenance of drug products, regulatory affairs can also play an important role during the early stages of the drug development process, advising on a number of historical and strategic issues.

This may include providing an Initial Opportunity Assessment (“what lessons from the past can we learn from?”) and Initial Product Profile (“what studies are needed, what issues will need to be discussed with the Regulatory Authorities?”). Prior to Clinical Trials, regulatory affairs may be asked for input regarding trial design (“Do we need to amend our targets based on toxicology studies? Have we agreed our development plan with regulators? Does the trial design meet regulatory/clinical end-points?”). Prior to submission, input may be required on such topics as labelling (“Do the data support the proposed labelling? What can we learn from a competitor’s experiences?”). Beyond approval, regulatory affairs will inevitably be advising upon how a product’s life-cycle can be managed to best effect.

With searchable access to documents associated with drug development and pre-clinical testing across drug classes, PharmaPendium® provides historical answers to all of the above. It provides an unprecedented level of data from which to investigate the potential repurposing of drugs, compare previous formulations, identify regulatory precedents within the drug class and learn from competitor's experiences. Furthermore, examination of previous approvals can yield important insights into experimental design and the statistical choices and models associated with these studies. "It's not necessarily what you know – more often than not it is a case of understanding where to get the information from" L.A.B. (Global Regulatory Consultancy Company)

Regulatory Cycling

The availability of local regulatory intelligence will ensure that the specific submissions requirements are met and the submission process fully understood. Only by proactively considering the submission strategy, submission requirements and necessary data and documentation can one avoid "regulatory cycling" – the time-draining dialogue between a company and regulatory authority during the approval process. By preempting and meeting an authority's specific requirement, a relatively efficient analysis of the product's Benefit/Risk ratio and subsequent approvability can be reached.

Access to this wealth of historical data enables the Regulatory Affairs professional to pre-emptively and proactively avoid the duplication of past mistakes made by others. Strategically, such data helps ensure that only the best and accepted experiments are submitted for regulatory review. Furthermore, exploration of the PharmaPendium® archives may yield similar cases which are available for citation may highlight a number of key regulatory precedents.

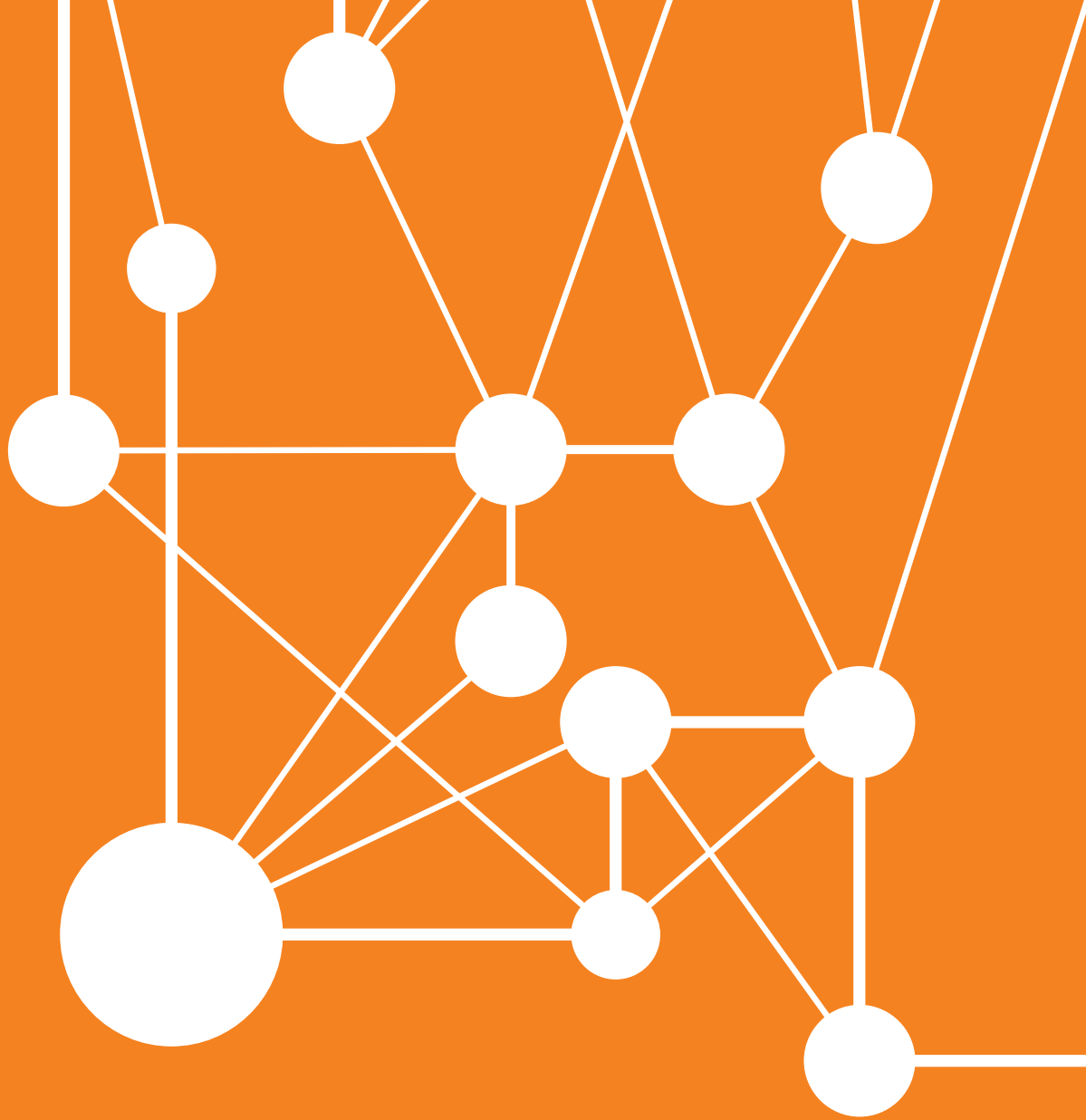
Ultimately PharmaPendium® provides an unrivalled opportunity to proactively learn from past approvals in order to streamline and accelerate the regulatory approval process. What makes a good submission? What were the reviewer's comments? What aspects were most effective? Is the submission package complete? Consideration of such questions can avoid the unnecessary process of regulatory cycling and facilitate a quick and effective approval process.

Paradoxically, whilst the pressure for a swift, successful drug approval process is as strong as ever, the prevailing environment within which this process is conducted is one of budget constraints, shareholder pressure, potential down-sizing/outsourcing of departments and ever increasing regulation and legislation. The pressure for regulatory affairs departments to do “more with less” has never been more prevalent – and therefore the Regulatory Affairs professional must use any available tools at their disposal to reach their approval goals. In terms of providing access to successful regulatory approvals packages, PharmaPendium® may well prove to be invaluable to the Regulatory Affairs professional.

Conclusion

As the profile of the Regulatory Affairs professional continues to grow within the Pharmaceutical Industry, the pressure to provide robust, high quality regulatory submissions steadily increases. PharmaPendium® can act as an important tool in this process, providing instant access to archived approvals, drug reviews, drug development data, comparative data and regulatory precedents. Such data can play an important role in shaping regulatory submissions on a global level by throwing the spotlight on previous submissions within a drug class, specific data requirements and the most successful approval packages. In particular, submissions via the increasingly popular US 505(b) (2) regulatory pathway (“Improved Generics”) can be strengthened with such data, leading to shortened approval timelines, reduced cost and market exclusivity of up to 5 years. However, irrespective of the chosen regulatory pathway, PharmaPendium® provides a unique opportunity to learn from the past in order to achieve success in the future.

Note: This interview was completed in 2013.



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