Regulatory Project Management: Landscape Analysis & Solutions

PHARMICA CONSULTING

ERIN TYNEBOR

Contents

Introduction

No one can deny the importance of Project Management and the value it brings to drug development. The pharmaceutical industry has invested heavily in this skill set, establishing project management centers of excellence and funding certifications and training for their employees. Even the smallest of companies will staff each drug development program with a project manager. The return on investment is significant, resulting in more focused programs and reductions in cycle times. And as we all know, shaving just days off the development timeline can equate to millions of dollars in additional revenue. Most companies have created additional specialized roles for Clinical Trial Managers and even Preclinical Trial Managers. It is also common to find Regulatory Coordinator type roles that apply project management to the authoring, assembly, publishing, and archiving of submissions. However, this is a very narrow minded view of what Regulatory Project Management should be. Organizations that aren't applying project management in the Regulatory space, beyond the very tactical tasks, are shortchanging themselves. Let me explain why there is significant value to be gained by applying project management in the Regulatory space in a much broader way.

There are several recent trends in the industry that we should explore first.

1. The realization that there are large and rapidly growing markets outside of the US, EU, Canada, and Japan.
2. The rapidly changing Regulatory environment in these new markets.
3. The constant search for cost savings on the manufacturing side.

1. Market Landscape

When researching the cloud, you will come across many definitions where most of it is just marketing lore. In simplest terms, the cloud can be broken down into:

Once upon a time, not long ago, product development teams were in a race to file their new product quickly in the US and EU. And once they finished that, they could take a deep breath and then begin thinking about additional markets. After all, most of those additional markets require approval in the US or EU prior to filing. Well those days are long gone. All major pharmas now recognize the importance of the largest emerging markets – Brazil, Russia, India, and China – but many are going far beyond that to establish a leading presence in 2nd and 3rd tier markets as well. IMS Health initially identified 7 "pharmerging" markets expected to grow more than 7.5% per year through 2011, to become 12% of the global market. Later their list expanded to 17 markets which will, in aggregate, expand by $90 billion during 2009-13 and contribute 48 percent of annual market growth in 2013. These additional markets include Southeast Asian markets such as Indonesia and other fast growing markets such as the Ukraine and South Africa. And finally, some companies have their eye on 3rd tier markets such as Sub-Saharan Africa where the market is small currently but have significant potential. Establishing a strong presence in these markets early will ensure a leadership position in time to capitalize on the growth opportunity.

So what does all this have to do with Regulatory? If you peel back the onion on these emerging markets, you find that they don't all require prior approval in the US or EU. And even if they do, perhaps you want to have your dossier ready for submission, just waiting for that approval letter or Certificate of Pharmaceutical Product. Finding innovative ways to reduce the cycle time to filing in these markets is

critical. This requires early discussions within the product development team to plan ahead. And it requires early discussion with the local regulatory experts who have an often untapped wealth of ideas and innovative strategies to bring to the table. Applying a project management skill set in this space to put very detailed submission plans together is an asset to any company that considers these markets to be a priority.

2. Regulatory Environment

The job of the regulatory professional just got harder with the expectations around all of these additional markets. But it doesn't end there. Not only are the economies in these markets rapidly evolving, but so are their regulations. The Health Authorities now realize that they are in a position of power and they are starting to flex their muscles. They aspire to be like the US and EU, implementing stringent regulations because they can. Do these Health Authorities actually have the resources and expertise to thoroughly review the submission? Not necessarily. Is it a box-checking exercise? It may be, but you don't have much choice but to comply or negotiate which, in many markets, is incredibly difficult.

Here are some good examples.

- CTD Module 3: Traditionally, most companies tailor their submissions in these non-EU/US markets according to their comfort with the protection of their intellectual property. Unfortunately, not all markets afford the IP protection that we have in the major markets. This means creating different versions of the CTD Module 3 for different markets or clusters of markets. These requirements change frequently as regulators raise the bar and require a greater level of detail.
- CTD Module 1: Requirements for country-specific documentation in the CTD Module 1 also change quite rapidly. Agencies are now asking for legalized documents, batch manufacturing records, certificates of analysis from suppliers, and on and on. There is a long list of documents that potentially make up the Module 1 for any specific country. Multiply that by 20+ countries and you have countless permutations of documents that are sourced from multiple places – manufacturing sites, suppliers, health authorities.
- Local Registration Studies: These are clinical trials conducted in the local population to determine if there are characteristics of the local population that result in a different safety or efficacy profile as compared to the global population. Russia, China, Taiwan, Vietnam, and other markets now require local patient data.

It would be nice if there was a simple recipe to follow. If I want to file product X in country Y, I have a specific list of exactly what I need and I can plan for it. However, in this rapidly changing environment, this approach is not realistic. A recipe may be a starting point but a good Project Manager can facilitate the dialog with the local country experts early on to set a plan, mitigate risks, and monitor it as the environment changes.

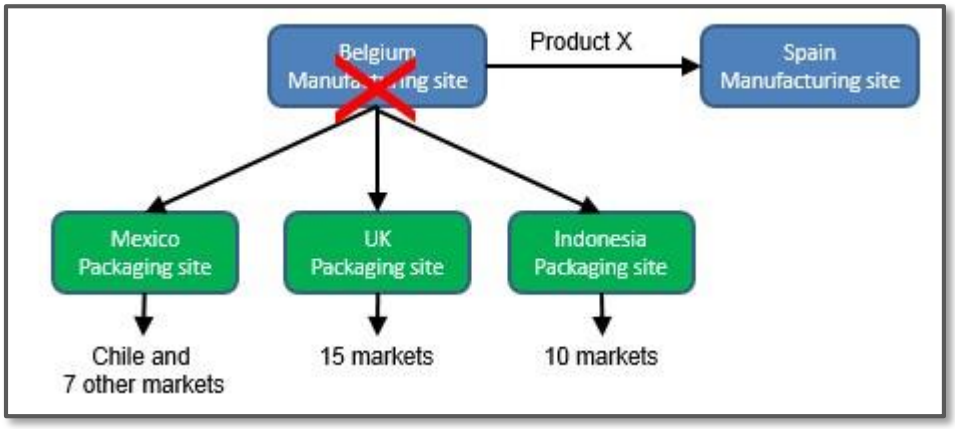
3. Manufacturing

As if the regulatory environment wasn't complicated enough, we have to pile on the added complexity of manufacturing. Companies are trying to cut costs everywhere and in the manufacturing space they are doing so by switching to low cost suppliers, outsourcing, or changing the manufacturing process to eliminate waste or increase output. Likewise, patients are demanding more affordable healthcare and

prescription drug costs are a big component of that. Price is actually a significant barrier to entry in emerging markets so all the more reason to find low cost manufacturers. The bad news is, all of these changes implemented by manufacturing can trigger a filing in the markets where that product is approved.

And there are actually more interesting factors at play aside from just cost cutting. Many countries incentivize companies to manufacture product locally. They may offer shorter approval timelines, less stringent filing requirements, higher pricing, first entry into the generic market, preference when bidding on tender opportunities, etc. Countries such as Russia, Turkey, Algeria, and Iran are offering these kinds of incentives. In these situations, companies are looking to either localize their operations or partner with a local manufacturer. The cost of doing so may be high but so is the reward. Developing a regulatory strategy and implementation plan in these situations can be quite complicated.

Let's consider what happens when you move manufacturing from one site to another. In the example below, we are moving Product X from a formulation site in Belgium to a site in Spain that supplies product globally to 33 markets. The goal is to get regulatory approval of the change in all 33 markets before they stock out of product manufactured in Belgium. For each market, you need to figure out what the filing requirements and timelines are and create a plan. Then work with your manufacturing colleagues who have their own timelines and constraints to come up with a plan that works for all and guarantees continuously supply of product to patients.



For each of the 33 markets you may ask the following questions.

- How long will it take to get the submission approved?
- What are the CTD Module 1 requirements? Remember, it's quite likely that all 33 markets have a unique set of requirements.
- How many months of stability data are required? Does it need to be site-specific? On how many batches?
- Do you require registration samples at the time of filing?
- Do you need prior approval in any reference markets?
- And on and on….

As you can see, it is a complex exercise and there is often a lot of back and forth negotiation and planning between regulatory and manufacturing to make the pieces fit together.

Solutions

It's clear that the Regulatory environment is impacted significantly by the demands of the business as well as the demands of the Health Authorities worldwide. So how does a Regulatory organization set itself up for success? Clearly the scientific expertise and depth of knowledge in the regulations is incredibly important. This much is obvious and most organizations aim to excel when it comes to regulatory strategy. But what isn't so obvious is that the strategy will fall flat without a good operational mindset. Strategy without operations is akin to identifying a goal without the defining the plan as to how you will get there. Project Management complements the regulatory strategy with the following skills.

- Management of project timelines and identification of the critical path.
- Identification and tracking of all deliverables and ensuring all team members are aware of their responsibilities.
- Identification of risks and creating a plan to mitigate them.
- Ability to resolve issues in a timely manner and escalate when necessary.
- Building alignment across team members.
- Facilitating effective communication across regulatory disciplines: strategy, labeling, publishing, etc.

Hence the need for Regulatory Project Management which could take many different forms. It's not necessarily an organization in and of itself. It's a capability and you have to choose how to deploy it. From an organizational design standpoint, there are two major options.

1. Embed the skills within existing roles or teams.

Small companies may have limited staff that wear many hats, whereas large companies may have specialized roles for strategy, regional expertise, labeling, publishing, etc. No matter what the organization looks like, if you choose not to establish a dedicated regulatory project management group, make sure that the skills are ingrained into an existing role or roles. Set expectations for these roles around planning and core project management skills. Require them to have project timelines by country, detailed tracking of components for each country, and meeting agendas that allow for discussion of these items and which are at risk. Also require them to have a mechanism for interfacing with other stakeholders, such as manufacturing and authors who contribute dossier content, to gain agreement to the plan. Training, definition of roles and responsibilities, development of sound business processes, and standard templates may be required to be successful with this approach.

2. Create a Regulatory PM organization

In a larger organization that has many Regulatory roles, large product pipelines, and a global footprint, it may be worthwhile to create a stand-alone project management function. This model may create some economies of scale and more robust PM best practices. It's no surprise that many CROs and consulting firms are now offering project managers with this expertise, which may be a smart move if internal head count is limited.

Defining how you want to implement a project management capability is the first step. Inevitably, the question of tools will always arise soon thereafter. Everyone wants tools and everyone has a vision of what the ideal tools may look like. Be realistic and keep in mind, again, the size of the product portfolio and global footprint of the company. How difficult is it to communicate submission plans and timelines

across the organization? How difficult is it to keep track of local filing requirements and the status of local submissions? In small organizations, this may not be much of a pain point but in mid to large size companies, this can become a lot more difficult. There are a multitude of options available to capture and communicate this information. Regulatory Information Management systems are quite popular and they may appear to be the magical solution. Keep in mind the true needs or your organization and your true requirements before deciding how elaborate your tools need to be.

As you consider ways to improve your operations or scale up your regulatory organization, do not overlook the value of project management. Think big, beyond the tactical tasks of tracking dossier components. The environment is rapidly changing and business needs are as well. As there are fewer and fewer blockbuster products entering the marketplace, companies are searching for other sources of growth which may mean expanding their global footprint both from a commercial and a manufacturing perspective. Your organization can adapt better to this changing environment by implementing project management practices and tools. Consider the size of the organization, the size of the product portfolio, and your geographic footprint when making decisions about organizational design, roles and responsibilities, and tools.