While the global pharma market is predicted to grow in coming years and seems to be entering a new phase of increased product approvals, life sciences firms are facing higher costs, associated with increased operational and regulatory complexity. Many in the industry seek to address these challenges by increasing the efficiency and effectiveness of Research and Development (R&D). However, in order to realize the full value of investments in R&D, it’s imperative to fix the product development lifecycle in areas downstream of R&D, in areas such as Regulatory Affairs Operations, quality, and manufacturing. Doing so will have at least as significant an impact on cost, margins, and revenue – if not more.

This white paper makes the case for transforming Regulatory Affairs Operations and for recognizing it as a critical component of the life sciences value chain, one that must be approached as strategically as R&D or clinical operations.

Optimizing Regulatory Affairs Operations is central to overcoming the challenges facing the life sciences industry. Specifically, improving document management, along with the process controls associated with regulatory submissions, has the potential to significantly reduce time to approval, thereby increasing the efficiency of the entire product development value chain and, ultimately, reducing time to market.
Introduction: Life Sciences at a Crossroads

The general consensus is that the life sciences are at a crossroads, but what the next 5 years hold is far from clear. It’s hoped that the high number of approvals granted in 2012 and 2014 (which seem to be continuing in 2015) herald a return to mid-1990s levels after the trough of 2001 – 2004, although historic big pharma has not recovered as well as the rest of the industry (see Figure 1). A significant number of high-revenue-generating drugs are coming off patent in the next 5 years, so this trend needs to continue to help recover the loss from these off-patent products.¹

If we turn to look at return on investment for approved drugs, the picture gets less rosy. The Pharmaceutical Research and Manufacturers of America (PhRMA) reports that only two of ten marketed drugs return revenues that match or exceed R&D costs², and a recent analysis argues that R&D spending by the largest pharmas has continued to grow at stunning rates.³

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¹ The leading pharmaceutical companies will lose between 14 percent and 41 percent of their existing revenues as a result of patent expiries by 2020 (PwC Pharma 2020).

² PhRMA 2014 Profile.

³ Data published by InnoThink Center For Research In Biomedical Innovation and Thomson Reuters Fundamentals (via FactSet Research Systems) suggest that the largest firms have spent an average of $4.8B per approved drug over the last 15 years (retrieved from http://www.forbes.com/sites/matthewherper/2013/08/11/the-cost-of-inventing-a-new-drug-98-companies-ranked/).
In the meantime, the life sciences market globally is predicted to grow 31 percent in the next 5 years, a healthy figure (see Figure 2). However, growth in the U.S., European Union (EU), and Japan is predicted to be only 13 percent in that time, while the growth in rest of world (ROW) is predicted to be nearly 50 percent, at which point sales between U.S./EU/Japan and ROW will be roughly equal. But this growth will be a mixed blessing at best, bringing increased operational and regulatory complexity, combined with far lower available spend per patient.⁴

And beyond these well-known challenges, the life sciences also face a range of emerging challenges that, while less certain than the patent cliff and eroding margins globally, are no less significant for the future of the industry: 3D printing; the increasing importance of large molecules and biosimilars; the evolving complexity of partnerships, joint ventures, and outsourcing; global electronic Common Technical Document (eCTD) submissions; Identification of Medicinal Products (IDMP) compliance; the desire of regulators to move away from documents to pure data (e.g. for Form 1572s); the quickening pace of collaboration between health authorities (HAs) across the globe; the shift from treatment to diagnostics; and the rise of personalized medicine – each of which presents its own challenges to the industry.

On the whole, wherever you stand on the challenges facing the life sciences and whether you take an optimistic or pessimistic view of where the life sciences are headed in the next 5 years, firms that hope to prosper have their work cut out for them in this dynamic and uncertain environment. Those that fail to adapt and address their challenges will continue to spend more money and expend more effort to realize flat (or even lower) gains.

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Figure 2: Projected Pharmaceutical Sales 2020 by Geographic Region (Source: Business Monitor International via PwC Pharma 2020 Website)

Source: Business Monitor International
Notes: (1), All sales are expressed in US dollars at constant exchange rates; (2), The growth markets include, in descending order of size, China, Brazil, Russian, India, Mexico, Turkey, Poland, Venezuela, Argentina, Indonesia, South Africa, Thailand, Romania, Egypt, Ukraine, Pakistan, and Vietnam. (3) EU-Big 5 is France, Germany, Italy, Spain, and United Kingdom

⁴ For instance, the U.S. spends $10,844 per diabetes patient per year; India spends $420 per diabetes patient per year (PwC Pharma 2020).
By and large, the prevailing wisdom of how to address these challenges is to fix R&D. Large consultancies such as KPMG and Pricewaterhouse Coopers (PwC), as well as industry organizations such as PhRMA, point to R&D as the main source of life science’s problems and its best hope of overcoming them: Life science organizations need to make the process of drug discovery more efficient and effective by finding greater numbers of promising new molecules, weeding out losing molecules as early as possible by “failing faster”, and by fostering partnerships to spread operating costs and spur innovation. In addition, overall portfolio management needs to become more mature and pragmatic, driven by risk and value rather than by organizational politics, to drive “losers” out of the pipeline sooner (Phase I and II) rather than later (Phase III).

However, it is Doculabs’ view that addressing R&D can be only one part of the solution, because the way in which viable molecules are moved through the product development lifecycle downstream of R&D will have at least as significant an impact on cost, margins, and revenue as the efficiency and effectiveness of R&D — if not more. Furthermore, the significant and necessary investment in R&D will deliver a smaller return if processes downstream aren’t also optimized.

In our work with life science organizations over the last two decades, Doculabs has seen that, compared to manufacturers in other sectors, life science organizations are typically very inefficient across the integrated product life cycle – not only “upstream” in R&D and clinical operations, but “downstream,” in Regulatory Affairs Operations, quality, and manufacturing. Lean principles and approaches are far less a part of the life sciences DNA than they are in practically any other manufacturing sector, except perhaps oil and gas.

It’s Doculabs opinion that Regulatory Affairs Operations is central to overcoming the many real challenges the life sciences industry faces in the next 5 years. It’s our view that life sciences firms must change how they view Regulatory Affairs Operations, transforming it from an administrative function to a strategic capability, and work hard to “lean out” their Regulatory Affairs Operations globally to bring products to market more quickly and efficiently.

This white paper presents Doculabs’ recommendations for transforming Regulatory Affairs Operations, based on our work with life sciences firms over the last two decades.

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5 Prominent examples of an R&D focus include PwC Pharma 2020, KPMG Future Pharma, PhRMA 2014 Profile.
The Importance of Regulatory Affairs Operations

The life sciences industry is a needle-in-a-haystack business – a business driven by massive amounts of effort to discover a single viable product. One way to improve success under these conditions is to try to find more needles, which is what the prevailing research from PwC, KPMG, and others recommends. The flip side, and the route that Doculabs finds more viable, is to work more effectively and efficiently with the needles you’re already finding.

Looking at the mathematics of the drug development funnel illustrated in Figure 3, the challenges of the focus on R&D become apparent: If 10,000 compounds lead to five drugs in trials to yield a single FDA-approved medicine, how could life sciences firms possibly increase the number of compounds they evaluate in the discovery phase to significantly impact these ratios?

Common sense would seem to suggest that they couldn’t; but even if they could, common sense also suggests that, as manufacturing organizations, life science firms should apply lean principles to the entire product lifecycle, not just a single phase. The problems facing the U.S. auto industry could not have been solved solely by making R&D more effective and efficient; the answer lay instead in bringing the products they already had in the pipeline to market more efficiently and with higher quality. The same holds true for life sciences today.

Consider this: If a global life sciences organization operating in 50 countries were to reduce the time to approval by 1 week in each country in ROW by improving Regulatory Affairs Operations processes (a conservative estimate, given how poorly many organizations manage regulatory documents or enforce global regulatory process standards), that would deliver 50 additional weeks of sales per product across geos.

Figure 3: Drug Development Process
In conversations with regulatory affairs professionals at recent meetings of the Drug Information Association (DIA) and the Regulatory Affairs Professionals Society (RAPS), Doculabs heard that typical regulatory delays due to poor document management tools and processes would be more like 4 to 8 weeks per country in ROW. For a company operating in 50 countries, that would result in from 200 to 400 additional weeks of sales per product – which would go a long way toward reversing the margin erosion due to increased sales volumes in ROW, as well as lengthening the time on patent, for example.

And these kinds of inefficiencies are not limited to Regulatory Affairs Operations. The time and effort expended to manage quality and manufacturing documents (particularly for device or combination product manufacturers) also lead to inefficiencies and delays at most organizations, and the upshot is slower time to market or lower margins (or both).

Yet despite the potential gains that areas like Regulatory Affairs Operations and quality present, life sciences organizations typically regard them as administrative overhead rather than as strategic capabilities, and fund them accordingly – i.e. at a significantly lower level than R&D, clinical operations, and sales.

Considering once again the figures cited at DIA and RAPS (admittedly unscientific and anecdotal), the potential savings from improved document management and process controls are staggering. As cited previously, a company operating in 50 countries would gain 200 to 400 weeks of sales per product, but for one operating in 100 countries, the gain is 400 to 800 weeks; in 150 countries, 600 to 1,200 weeks. Even taking a conservative stance and estimating a single week of savings per regulatory submission in each country, the numbers are compelling: 50, 100, and 150 weeks of sales, respectively. Multiplied across a portfolio of products, these numbers become even more persuasive.

Given all this, it’s difficult to see how life science organizations can justify continuing to ignore the importance of Regulatory Affairs Operations to their financial performance. It’s Doculabs’ view that the firms that do so (by overly-focusing on R&D performance, for example) will fare far worse in the next 5 years than those organizations that learn from their manufacturing counterparts in other sectors and work to lean out their entire product development value chain – and a significant part of those efforts will need to be devoted to improving Regulatory Affairs Operations.
Regulatory Affairs Operations Efficiency

Regulatory Affairs Operations is all about information: gathering it, collating it, transforming it, and transmitting it. Without strong information management processes and capabilities, Regulatory Affairs Operations is dead in the water: It will take longer to get products approved, with greater effort and with lower quality. And this problem is only magnified for global organizations that are seeking regulatory approval in dozens, if not hundreds, of countries.

Figure 4 illustrates a fairly representative regulatory submission process.

At each step of the way, managing controlled documents – e.g. labeling, company core data sheets (CCDS), source documents, records of communication with agency, agency questions and responses, etc. – is at the heart of what Regulatory does. So considering how poorly most life sciences organizations manage their regulatory submission documents in ROW, it’s not surprising that many global Regulatory Affairs Operations groups are less efficient than they could be.

So what does an efficient Regulatory Affairs Operations function look like, at least from a document management and process efficiency standpoint?

First, it has a common repository in place, to hold all regulatory documents. This repository provides version control, check-in/check-out, and rudimentary authoring and approval workflow, as well as the basic metadata (or “tags”) required to make the documents findable. At a minimum, such capabilities allow employees working on submissions in different countries to share key documents and information easily and effectively. At more mature organizations, these capabilities may be extended to include structured authoring and publishing capabilities that enable a “virtual dossier” approach, i.e. the ability to reuse content chunks and to group stand-alone documents into submission packages without having to physically group the documents together or make copies.
Second, in an efficient Regulatory Affairs Operations function, there’s awareness that Regulatory Affairs Operations in each country require different documents, so it’s paramount to deliver submission dossiers in “chunks” – i.e. not as single, multiple-thousand-page PDFs that each affiliate has to slice and dice to create its submission. Rather, hand over dossiers made up of multiple PDFs, tagged accurately, so that each affiliate can find what it needs quickly, use it in its submission, and ignore the rest.

Finally, in this efficient and effective Regulatory Affairs Operations function, there is a recognition that Regulatory Affairs Operations can benefit from process standardization across geos. This is not to say that there won’t be differences between how Regulatory Affairs Operations functions in Vietnam versus in the U.S, for example, but rather that the differences shouldn’t lull us into ignoring the many significant process improvements to be gained by standardizing relevant portions of the submission process.
The Strategic Transformation of Regulatory Affairs Operations in Life Sciences

The Way Forward

Although the situation at every firm is different and will require an individualized approach, there are some common, high-level activities that firms should engage in to address the Regulatory Affairs Operations challenges we've presented in this white paper. The approach below is one that Doculabs has used successfully not only with life sciences firms, but with Fortune 500 firms across nearly every industry in the last 20 years.

1. **Build a program.** Approach document management as an ongoing program rather than a one-off effort or technology play. A key success factor is including stakeholders from across the enterprise, not simply one function or department – e.g. IT, Legal, and Records Management in addition to Regulatory Affairs. In many situations, widening the circle to include upstream and downstream stakeholders, such as clinical, R&D, commercial, quality, manufacturing, pharmacovigilance, etc., can provide additional benefits.

2. **Assess where you are.** It’s important to take stock of where you are in terms of managing submission documents globally. While many firms are up and running with electronic submissions in the U.S. and EU and therefore quite efficient in these regions, in ROW things are anything but. And while most large firms have an enterprise document management system in place for Regulatory Affairs Operations, the value delivered by these systems varies widely, as does the adoption rate. Unless you clearly understand your current state, you'll struggle to define where you want to go – and to get there.

3. **Decide where you want to go.** Once you know where you stand with managing submission documents globally, you need to decide where you want (and need) to go in the next 3 years. And this shouldn’t be solely about technology, or even solely about Regulatory Affairs Operations; it should be about how Regulatory Affairs Operations can support the larger strategic goals of the whole organization, by improving how it manages submission documents globally.

4. **Determine how to get there.** Getting from Point A to Point B requires a plan for how to get there. In order to move your ability to manage submission documents globally from where you are today to where you want to be tomorrow, you need a roadmap of the activities required to make progress. Typically, this roadmap will be holistic, addressing not only the technology changes, but the people and process ones as well: for instance, policy work, change management, training and communication, process improvements, and information architecture (taxonomy) development.
Conclusion

In the short term, life sciences firms should address inefficiencies in Regulatory Affairs Operations in a focused way: through improving how they manage regulatory submission documents globally, as we argue in this white paper. Doing so, they will realize significant benefits from standardizing the submission process and providing baseline document management and collaboration capabilities to affiliates. Tactical improvements such as these will likely shorten the time to submission by 1 week per country, at a minimum.

Life science organizations can then begin working to realize the larger strategic value that Regulatory Affairs Operations can provide by contributing to enterprise-level activities such as the following:

- **Product lifecycle management (PLM):** Regulatory context and timelines affect development and launch schedule, as well as the resources (time and money) required to bring individual products successfully to market.

- **Portfolio/pipeline management:** Regulatory context and timelines affect development and launch schedule of the entire product portfolio, as well as the resources (time and money) required to bring the portfolio successfully to market.

- **Product innovation:** New products and manufacturing techniques (such as 3D printing and combination devices) require regulatory innovation through collaboration with regulators, competitors, and others in order to be viable.

- **Mergers and acquisitions:** Without full understanding of the regulatory context, merger and acquisition activity is less effective and efficient and (ultimately) less successful.

Realizing the full value from Regulatory Affairs Operations requires not only an efficient and effective Regulatory Affairs Operations function, but recognition that Regulatory is more than an administrative activity: It’s a critical component of the life sciences value chain that must be approached as strategically as R&D or clinical operations.
About Doculabs

Doculabs, Inc., is a strategy consulting firm; our clients rely on us to help them improve the way they manage information. We provide services such as the development of strategic roadmaps and business cases, program management design, and content migration assistance.

Our consultants are experts in helping clients manage content such as Office documents, web content, email, customer communications, and records to improve operations, lower costs, increase revenue, and reduce risk.

Doculabs has in-depth expertise in information management across a range of industries, including life sciences, manufacturing, financial services, insurance, and energy. Our recommendations are based on our experience and our empirical data from hundreds of consulting engagements over more than 20 years. As trusted advisors that do not sell technology solutions, we provide completely objective services and recommendations.

In our 20-year history, Doculabs has helped many life sciences organizations to manage key information to improve their processes and their decisions, and to ensure effective regulatory compliance.

For more information about Doculabs, or for further information on the business problems discussed in this white paper, visit the web site at www.doculabs.com or call (312) 433-7793.