Lachman CONSULTANTS

WHITE PAPER

What you don't know CAN hurt you

LACHMAN CONSULTANT SERVICES, INC.

1600 Stewart Avenue
Westbury, NY 11590
United States
www.lachmanconsultants.com

HIGHLIGHTS

Why Regulatory Surveillance is Worth the Effort

1. The cost of reactive regulatory compliance is daunting, erodes credibility with customers and employees, reduces time to market and limits future strategic options.
2. The risks of non-compliance increase with the distance from market, length of supply chain, and number of markets.
3. Regulatory missteps in one market raise the concern of agencies in other markets, and therefore scrutiny.
4. Investing in staying informed – i.e. regulatory surveillance - is a simple step towards a sustainable strategic advantage of any life sciences company.

OVERVIEW

The global life sciences market is witnessing an unprecedented pace of change across pharmaceuticals, medical devices, and biologics. It's the new normal as trends like big data, the Internet of Things, increasing supply chain complexity and the advance of biosimilars create new opportunities – and challenges – for life sciences companies. As regulators around the globe scramble to stay abreast of these trends, they are making important and often major updates to directives. Quite often these directives are not coordinated between markets, creating a patchwork compliance landscape to be navigated.

If you are involved in your company's quality, regulatory surveillance, compliance, or knowledge management efforts, the following questions are for you:

Do you have frequent (i.e. at least monthly) conversations with the regulators in the markets where you manufacture AND sell?

Does your company have the expertise to predict and interpret regulatory directives?

Do you have reliable methods of disseminating information on the impact of regulatory directives to your clinical operations teams?

How does your organization remain aware of and respond to GxP actions, import alerts, or other market actions against other companies in your industry?

There is a sustainable strategic advantage to being armed with up-to-date knowledge of changes by regulatory bodies around the globe. By disseminating and integrating these insights, chances are you and your organization will get to market faster and maximize your time in market once there.

THE SEASCAPE OF REGULATORY TRIGGERS

Today's regulatory environment might best be described as a seascape. Using the alternative term 'landscape' would infer relative stability. Today's environment is frothy, full of what appear to be unpredictable currents, and for many, limited clarity as to what's going on underneath the surface.

So, what are the triggers of this ebb and flow? There are many, but the following three trends are most instructive.

GROWTH OF DATA

You have most likely heard of 'Big Data'. It is a non-specific description of the potential value to be found in collecting reams of data from anything with a sensor or digital footprint, then analyzing and utilizing that data for new applications.

Data Integrity

In the life science realm, the enormous growth in data being produced, analyzed, and communicated is forcing regulatory agencies to respond. One response has been to focus resources on data integrity ("DI")[1]. As an example, The U.K.'s Medicines and Healthcare products Regulatory Agency ("*MHRA")* report on inspections in 2013 highlighted an increase in DI issues while announcing the agency's heightened awareness in searching for such issues[2]. Of 630 GMP inspections in 2013, 216 showed major or critical deficiencies3. According to the MHRA, DI issues have been the key reason for a growth of critical deficiencies since 2013.

Across the Channel in Europe, the European Medicines Agency ("EMA") conducted 50% more GMP inspections in first half of 2015 than same period in 2014[4]. Their inspectors have also revised their approach to inspecting data integrity, utilizing data forensics experts to aggressively hunt for issues[5]. The U.S. Food and Drug Administration ("FDA") is doing the same.

Internet of Things

Another trend that is pressuring regulatory agencies to respond goes hand in hand with Big Data. Commonly called the Internet of Things ("IoT"), it refers to the massive growth in internet-connected objects that provide data outputs and react to data inputs.

A primary area of regulatory concern vis-à-vis IoT is cybersecurity. As supply chains grow and become more complex, risk managers are scrambling to get ahead of cybersecurity risks. Just ask your colleagues in IT. Major medical device manufacturers may have over 1,000 suppliers for a given portfolio of products. Each interface and data hand-off increases the risk of data theft, data integrity, or other cybersecurity issues. The risk is of such concern that the U.S. Department of Health and Human Services Office of the Inspector General has identified medical device cyber security as a principle area of focus in their 2017 work plan[6].

---

[1] For more information, see "The Real Cost of Poor Data Integrity in Pharmaceutical Manufacturing" March 2016, published by Lachman Consultant Services, Inc.

[2] "GMP Inspection Deficiencies 2013", 2014, UK Medicines and Healthcare Products Regulatory Agency (MHRA)

[3] Ibid

[4] "EMA Mid Year Report 2015", October 2, 2015, European Medicines Agency (EMA)

[5] Ibid

[6] "Top Management and and Performance Challenges Facing HHS", 2016, Office of Inspector General, U.S. Department of Health & Human Services

ECONOMIC PRESSURES

Regulators often take action against an industry when multiple players are thought to have poor quality management, a lack of attention to regulatory principles, or other systemic flaws.

Increasing competitive pressures typically lead to shrinking margins for most life science companies, often leading to reduced spend in quality management. Reduced spend increases the likelihood of quality deficiencies due to these cost reduction measures.

To illustrate, consider the generic pharmaceutical market, where competition has increased significantly across many drug categories. The number of pharmaceutical firms entering the market grew at 7.7% per annum from 2010-2015[7], while generics' percentage of the overall drug market grew to 87.5%, putting pricing pressure on the overall market (Figure 1).[8]

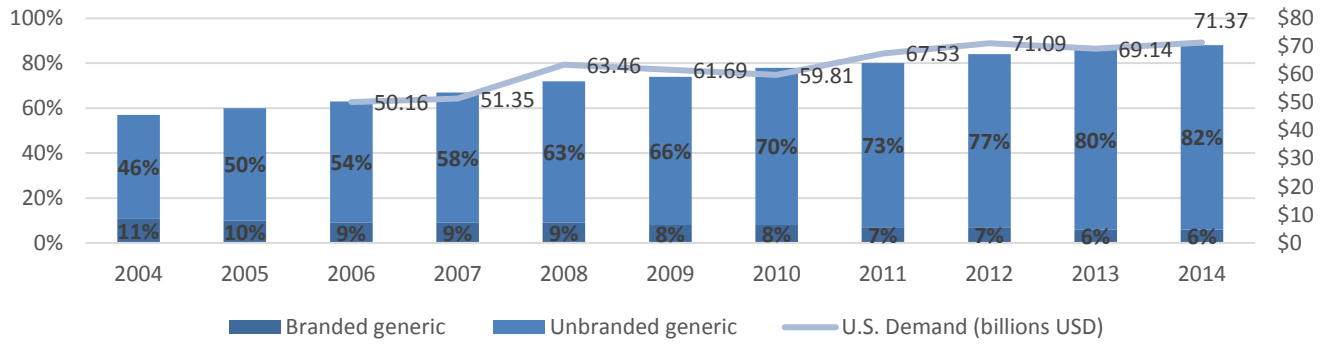


Figure 1: Generics as percentage of total U.S. retail prescriptions

Similarly, medical device manufacturer margins are feeling a squeeze. Public medical device company EBITDA margins fell from from 15.65% in Q2 2015 to 8.18% in Q2 2016 (Figure 1).[9]

As in any industry, margin pressures drive the need for greater efficiencies for manufacturers. Particularly for smaller companies, efficiency gains in the absence of revenue growth may often lead to cutting corners on R&D and design while chopping supplier, material, and personnel costs. All of these steps increase regulatory risk.

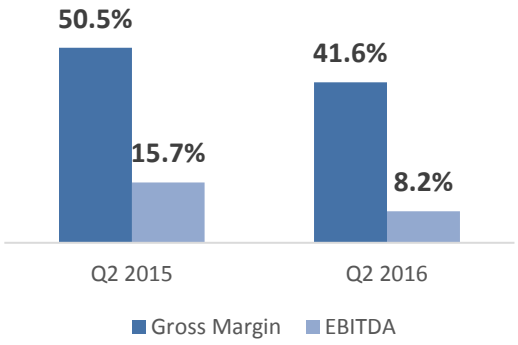


Figure 2: Medical Device Industry Margins

SHIFTING THE BURDEN

Let's face it. Regulators have a tall task. With today's pace of technology change, the blurring of lines between consumer products and regulated products, and the increasing complexity of bringing a life

[7]" IBISWorld Industry Report 32541b: Generic Pharmaceutical Manufacturing in the US, published Sep 2015

[8] Ibid, and "National Prescriptions Audit 2015", April 2015, IMS Health

[9] Compiled from public company data: http://csimarket.com/Industry/industry_Profitability_Ratios.php?ind=804

science product to market, how does an agency do its job?

Like it or not, regulators are responding by shifting more burden onto the life science company. We call this the 'Prove Innocence' approach. It is a philosophical change in part due to the demands mentioned above.

In the case of the FDA, the agency won't waste resources reviewing applications where there is a question of reliability. If the FDA feels an applicant's processes, adherence to processes, or reputation is not pristine, the FDA will require additional assurances to prove lack of 'guilt'. **Many recalls are now based on "lack of assurance" of GMP, as opposed to the presence of specific GMP issues.**

Furthermore, currently, if an individual facility is found to have compliance issues, regulator actions are not limited to that facility. Increasingly the entire life science company is held responsible for compliance issues. No matter the location or sub-entity that may own that facility, the corporate owner is now held responsible. This of course has significant implications for finance, operations, supply chain, and compliance.

In addition to the 'Prove Innocence' shift, the FDA has implemented Program Alignment which is organizing FDA into commodities based programs. This will result in a facility being inspected by an investigator with deep, specific experience in that product or compliance area regardless of geography.[10]

Why Your Company May Be at Risk

Let's start with agreeing that regulatory delays can have tremendous impact on even the largest manufacturer's profitability. For example, regulatory delays that impact a generic manufacturer's first-to-market entry, and the 180 day exclusivity period that comes with it, can significantly reduce profitability of that compound due to increased competition, as shown in Figure 3.[11]

Additionally, since regulatory action is based on the facility, and not the product, the effect of regulatory delay could be multiplied across the products being produced at that facility.

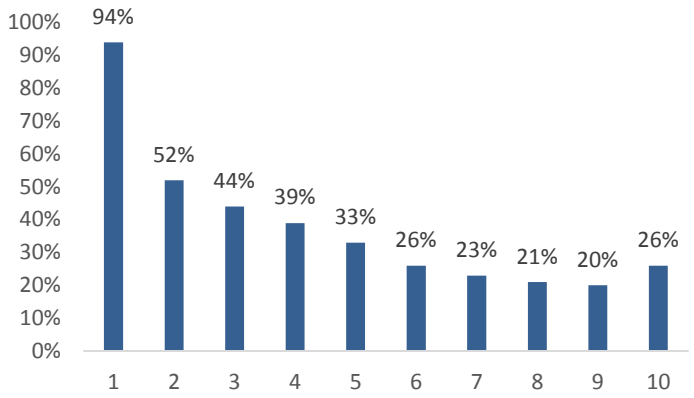


Figure 3: Generic Price per Dose by Number of Manufacturers in Market

In our experience in working with thousands of life sciences companies, **timely regulatory intelligence** is a key variable in managing regulatory risk. However, **regulatory surveillance is rarely a proactive and coordinated effort.**

Here are some reasons why. Do any of these seem familiar to you?

- For many companies, regulatory functions are seen as a cost center and a burden, particularly when profitability pressures lead to short-term, tactical decisions at the expense of longer-term, pre-emptive decisions.

[10] U.S. Food and Drug Administration, –" FDA Program Alignment", https://www.fda.gov/AboutFDA/CentersOffices/ucm392733.htm; last updated October 30, 2017

11 FTC Working Paper #317, April 2013, "The Effect of Generic Drug Competition on Generic Prices During the Hatch-Waxman 180 Day Exclusivity Period"

- Many companies operate under an assumption that regulatory functions are by definition reactive.
- In today's globalized life science industries, the markets where a product is sold are not the company's home market, meaning the company's personnel typically have limited experience with the regulatory bodies of the markets where products are sold.

> ***Timely Regulatory Intelligence***
> *Is a key variable in reducing regulatory risk*

- For regulatory surveillance professionals, it's very difficult to harvest the information that is available into useful bites. There is a tremendous amount of publicly available information, but very little analysis. In addition, obscure or small market areas are under-reported by most news sources, and there is little uniformity in interpretation of regulations.
- Knowledge management is stretched in larger organizations and regulatory compliance often takes a back seat to competitive and product related information. Without access to up-to-date info, misinformation (or information asymmetry) is more likely to spread amongst disparate groups.
- With increased supply chain complexity, suppliers' level of self-vigilance and willingness to be forthright about their own regulatory compliance challenges becomes extremely variable and difficult to manage.

A Solution

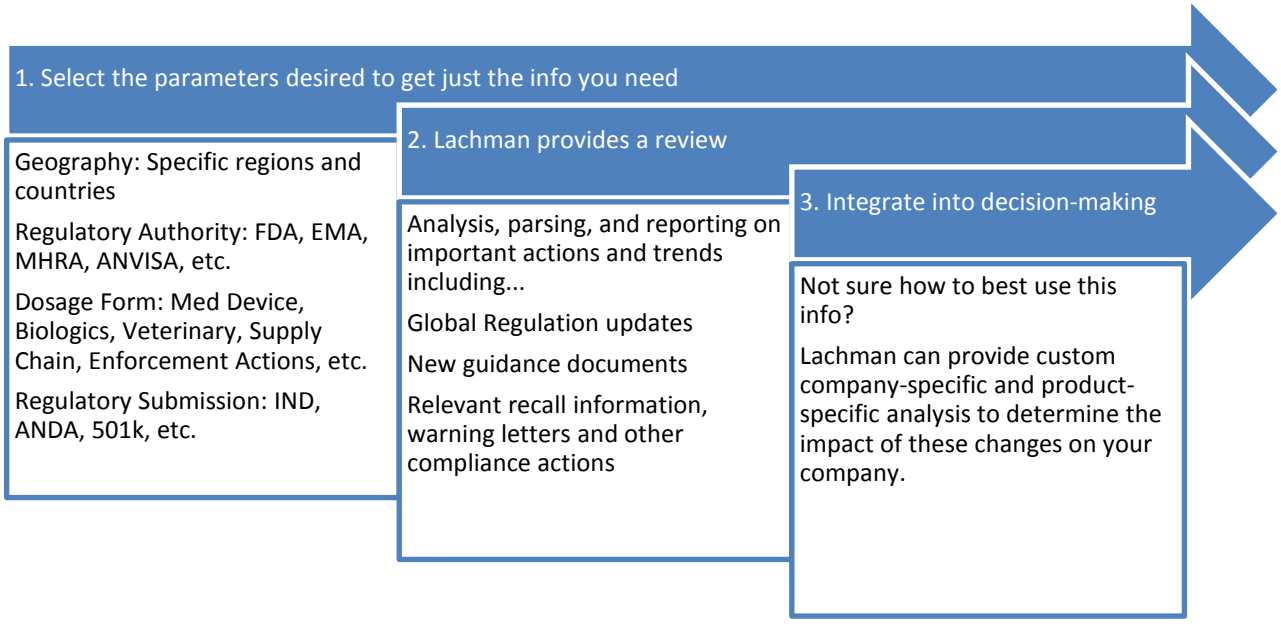
To help you augment and improve your regulatory surveillance efforts, Lachman has a solution. Lachman has worked with clients and agencies around the globe, and understands both the letter and spirit of regulatory updates from these agencies.

The Solution: We have developed a comprehensive, periodic summary of key regulatory and compliance issues, tailored to your business and markets.

The Benefit: To provide you with early and consistent access to better enable you to make decisions on process, procedure, and direction.

In many markets, visibility into future regulations is unclear. Being on top of trends is the only way to gain enough visibility to make an educated prediction. Our solution provides decision-makers with quick access to information.

Here's how it works.



There are several areas in your organization that may benefit from getting ahead of the regulatory curve and understanding the impact of actions and trends (see Figure 4). The most successful companies proactively monitor and manage regulatory forces in order to shape strategy. Lower performing companies limit this to tactical compliance.

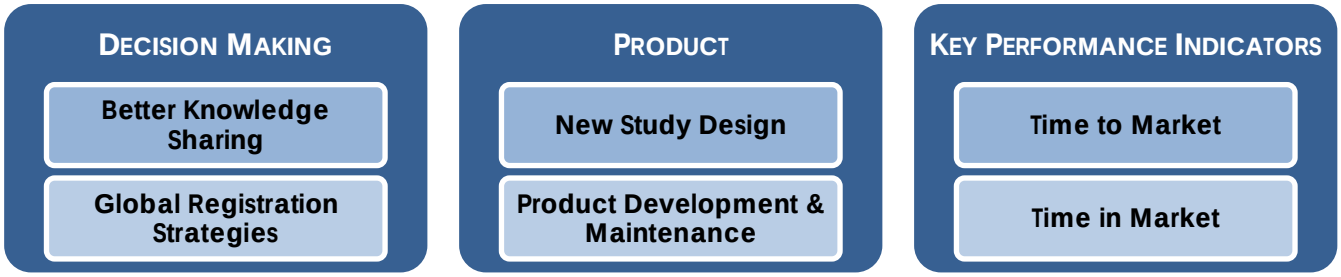


Figure 4: Organizational Impacts of Improved Regulatory Surveillance

STRATEGIES TO THRIVE

The decision on how to approach regulatory compliance is a strategic one, and varies based on the size and state of your company. It's a risk/reward decision. However, given the pace of change and challenges faced by regulatory bodies around the globe, a proactive regulatory surveillance strategy is part of a **sustainable competitive advantage**.

Compliance is an investment, and regulatory surveillance done right can create a sustainable competitive advantage.

There is a cost to waiting as opposed to acting now. The need to be proactive (i.e. strategic) is more important now than it was just a couple of years ago. Pulling all levers that optimize speed to market and maximize time in market are a must if a company is to survive.

Additionally, fighting regulatory fires is distracting, making it impossible for companies to be strategic. Without a step-change approach, once a firefighter, always a firefighter.

We have found that those companies which have accepted that **regulatory surveillance is an investment**, rather than an accounting cost center, are those that should expect to stay competitive in a tough marketplace. Investing in a system of accurate, effective, and sustainable compliance will protect profitability and shareholder equity in the long run, as well as serve to maintain brand equity amongst customers.

This requires a mindset shift from being a victim to the winds of regulatory demands to proactively managing those demands. Many warning letters point to poor or non-existent preventative actions. **Regulatory vigilance is a preventative action.**

BEST PRACTICE RECOMMENDATIONS

Limit your risk of lost sales and compliance issues. Start with the following:

REPORTING

Invest in a reliable source of regulatory updates and reporting, as well as its analysis.

KNOWLEDGE MANAGEMENT

Get this info in the hands of your sites, product groups, compliance and GxP owners, and supply chain managers by establishing scalable knowledge management triage and dissemination strategies to ensure this information is provided to the right groups at the right time.

WE CAN HELP

To better understand your risks and adequacy of your regulatory surveillance capabilities, contact us. We will explore how your company can gain or retain a sustainable competitive advantage through our services.

In addition to our regulatory surveillance solutions, Lachman also offers the following services to the life sciences industry.

AUDIT

Gap Analysis & Preparation for inspection or as a proactive quality step

TRAINING

Proactively ensure strong QSR training & corporate culture training in advance of a problem

ENHANCEMENT

Upgrade procedures and policies, address inspection observations or regulatory deficiencies identified in audits

SUSTAINABILITY & CONTROLS

Ensuring adequacy of staffing, internal and external audits, metrics and continuous improvement

PLANNING

Develop SOPs, risk-management plans, and quick response to inspections and regulatory actions

DUE DILIGENCE

Evaluation of compliance or regulatory status in preparation for potential M&A activity (buy-side and sell-side), including supplier evaluations

NEW PRODUCTS

Training and assistance with submissions, acting as US agent for offshore activities, facilitation with regulatory bodies

To start the conversation, contact

Linda Evans O'Connor, Head of Business Processes and Regulatory

at 516-222-6222 or

l.evansoconnor@lachmanconsultants.com.