

Global regulatory affairs—role in the biopharmaceutical industry

- 2.1 Overview
- 2.2 Global regulatory affairs organization
- 2.3 Role of global regulatory affairs
- 2.4 Key regulatory functions and activities
- 2.5 Global regulatory strategy
- 2.6 Global regulatory agency interactions

2.1 Overview

The regulatory landscape has continued to evolve in response to product safety, regulatory compliance, new technologies, improved understanding of disease states, stakeholder and customer needs and global imperatives, with new and increasing regulations, regulatory guidance and oversight. The global regulatory affairs group and the regulatory professionals in the biopharmaceutical industry occupy a central and pivotal role to all the functional groups. The regulatory team is charged with a strong leadership role that ensures compliance with regulations and enables understanding and interpretation of the dynamic regulatory landscape, while creating opportunities in the highly-regulated and complex environment.

The challenging landscape is largely a result of the success of the biopharmaceutical industry in delivering medical therapies for many disease states, safety catastrophes from use of products post-approval; and product quality compliance issues. These have sharpened regulatory authorities' focus on product benefit/risk profiles and related stakeholders' views on cost effectiveness and patient access. The regulatory professional has to be equipped and poised to effectively guide the organization to success with a credible voice, informed strategic guidance and objective evaluation.

The demand for globally acceptable products heightens the imperative for harmonization of regulatory requirements to lend efficiency and cost effectiveness to the process of product development, manufacturing and expediency to global access. In addition, biopharmaceutical companies have continued to expand their frontiers to attain a global reach, with presence in many regions and countries, and therefore exposed to myriad, and sometimes diverse, regulatory requirements and operating standards. The challenges of globalization in a heterogeneous world with an evolving regulatory landscape and expectations of multiple stakeholders have increased the complexity, unpredictability and intensity of the biopharmaceutical product development and registration process. These challenges likewise reinforce the crucial role of the regulatory team and underscore the need for enhanced global regulatory function with regulatory professionals who are strong leaders, business partners and strategic contributors.

The scope of the regulatory affairs group function spans the entire spectrum of product development, manufacturing, registration, post-marketing activities and lifecycle optimization. This span of involvement and responsibility is sometimes referred to as bench to bedside and beyond, from cradle to grave, from inception through lifecycle optimization, from laboratory to launch, etc. The regulatory team and professional hold a unique position of importance with impressive diversity in function and significant breadth and depth of responsibility.

This chapter focuses on the role of the global regulatory affairs team in the biopharmaceutical industry and draws upon its crucial and unique position to highlight the strong leadership

The biopharmaceutical industry is highly regulated by regulatory authorities across the globe.

Evolution in the regulatory profession has been largely driven by:

- Expanding scope and global reach of industry
- Keen attention to global regulatory intelligence
- Need for innovative, cutting edge technologies including e-submission
- Complexity of disease area targets for development
- Need for comprehensive and robust global regulatory strategies, all demanding highly skilled regulatory professionals with expertise, broad leadership and strategy capabilities.

function, critical business partner, strategic contributor and honest broker for some of industry’s most important decisions.

2.2 Global regulatory affairs organization

Functional units

Key functional units

- Product development
- Chemistry, manufacturing and control
- Policy and regulatory intelligence
- Regulatory submission
- Product labeling
- Promotion and advertising

Global regulatory affairs groups in industry provide worldwide, strategic leadership in and comprehensive direction of the government regulatory requirements for product introduction and commercialization, utilizing regulatory knowledge to ensure compliance and regulatory intelligence and create opportunities in a highly-regulated environment.

The global regulatory affairs group has strategic and operational functions, both requiring precision and flawless execution, as a company’s success relies on, in part, the guidance and rigorous assessment provided by the regulatory affairs team. The key product development, manufacturing and registration milestones (such as Investigational New Drug filing, end of phase II, phase III, New Drug Application submissions, regulatory agency review timetable and product approvals), which are the corporate valuation and decision points, are based on critical regulatory interface goalposts and milestones. This underscores the importance of strategic regulatory contribution to the industry. In order to be valuable contributors and critical business partners, the global regulatory affairs organization must develop mechanisms and establish systems to ensure it has the right people and talent, proficient processes, prolific productivity, phenomenal performance and precision in planning.

Table 2.1 Global regulatory affairs

Product Development Areas HQ & Regional	CMC, Compliance, Conformance	Policy & Regulatory Intelligence	Promotion & Advertisement	Regulatory Submissions Management	Product Labeling
<ul style="list-style-type: none"> • Develop and lead global regulatory strategy • Coordinate with regional regulatory teams for global strategy • Liaison with regulatory authorities • Review regulatory submissions 	<ul style="list-style-type: none"> • Liaise with BOH’s on CMC issues • Develop regulatory strategy for manufacturing plans/process • Support site and facility inspections • Conformance • Compliance 	<ul style="list-style-type: none"> • Monitoring for emerging trends, policies, regulations and guidelines • Analyze and communicate • Regulatory intelligence • External industry participation 	<ul style="list-style-type: none"> • Generation of competitive and compliant promotional materials • Regulatory review of promotional copies and publication • Primary liaison to regulatory agency on promotions and advertising 	<ul style="list-style-type: none"> • Electronic publishing and compilation • Document standards • Electronic CTD submissions • Technology management • Assembly of submissions 	<ul style="list-style-type: none"> • Develop product labeling • Ensure compliance and accuracy of product label
STRATEGY					
LIAISON					
GATEKEEPER					

What comprises global regulatory affairs

The global regulatory affairs groups within different pharmaceutical companies have different organizational structures and functional reporting. However, most are comprised of fundamental units that house the various specialists or experts within the regulatory function. The global regulatory affairs group has traditionally resided within the research and development group of biopharmaceutical companies, but that, too, is evolving. Many companies have recognized the central role of the group to all technical functions—development, manufacturing and marketing—and therefore are aligning the group’s reporting to a central and neutral executive. In some companies, the global regulatory group reports to the Chief Execu-

tive Officer—a statement of the importance of this function. The typical functional units are represented and may vary from company to company; therefore, this chapter will address the typical functional units of importance.

The key functions of the global regulatory affairs group include:

- Leading and providing strategic regulatory guidance and delivering the global regulatory strategy for product development, manufacturing and registration
- Building and maintaining a credible relationship with regulatory authorities with effective written and verbal communication
- Establishing an efficient repository and archive for correspondence compliant with regulatory standards for audits
- Providing high-quality, complete user/reviewer-friendly documents electronically transmissible and reproducible
- Developing and maintaining product information and label
- Providing regulatory intelligence, from paying attention to regulatory environment and changing landscape, to participating in external industry partnerships and developing policy with regulatory agencies
- Ensuring published information and promotional/advertising material meet regulatory requirements
- Ensuring functional units comply with regulatory requirements and good regulatory practices.

With the understanding of the key functions of the global regulatory affairs group, the structure is designed to assure successful execution of the function. The typical key functional units include:

The *Product Development group* comprises the regulatory technical experts that lead strategic guidance on product development, manufacturing, registration and maintenance in the market. This team develops the global regulatory strategy and regulatory authority engagements relevant for successful product development and registration outcomes. It reviews the documents for submission to regulatory authorities and is typically the primary point of contact for communication with the regulatory authorities for the company. Its members are referred to as regulatory strategists, liaisons, scientists or other lexicons to convey their role and the technical contribution they provide to product development, manufacturing and registration.

The *Chemistry, Manufacturing and Controls (CMC)/Conformance/Compliance team* has a similar function to the product development team, focused on the manufacturing process development and registration and manufacturing facility and site inspections. It ensures compliance to current good manufacturing processes; good laboratory and clinical practices; and audit compliance and readiness for regulatory inspections of the laboratory, clinical and manufacturing facilities and information technologies.

The *Policy and Regulatory Intelligence team* is increasingly important to product development, manufacturing and registration strategy. This team monitors the global regulatory environment for emerging trends, participates in creating policies, contributes company positions to regulatory agency guidelines and analyzes and assesses precedents and standards to provide intelligence and anticipatory input to enable robust, proactive regulatory strategies.

The *Promotion and Advertising team* works closely with the product development teams and the marketing teams to ensure competitive yet compliant promotion and advertising communication materials. It represents the primary liaison with the regulatory agency on promotional and advertising materials.

The *Regulatory Submissions team* is responsible for assembling, publishing and dispatching the regulatory submissions to the global regulatory agencies. It is at the cutting edge of new electronic technologies to ensure user/reviewer friendly, complete and navigable submissions. Its strategic focus and application of electronic technologies in the assembly of the dossier, from technical authoring groups to careful coordination of global requirements for electronic submission, enable expedient and near simultaneous submissions to global regulatory agencies.

The *Product Labeling team* is integrally positioned with the product development regulatory teams that provide strategic direction in the development of the label content with other technical team members. The product labeling team is responsible for developing the label package insert and literature, container labels and packaging, and updating the product information. This team coordinates the label content reviews by the relevant technical teams for accuracy and ensures compliance to the specific regulatory agency format and timelines for submission of the label information.

Global regulatory affairs functions play an integral role in the process of developing, manufacturing, registering and introducing safe and effective health-care products worldwide, with strategic planning, pre- and post-approval responsibilities, internal and external interfacing and communication as key responsibilities (RAPS 9/08).

2.3 Role of global regulatory affairs

The enhanced role of the regulatory affairs professional

The past 10 years have brought both an exciting evolution and challenging times for the biopharmaceutical industry with an increasingly complex and demanding regulatory environment, creating opportunities for both the regulatory profession and the pharmaceutical industry. This evolution in the regulatory function has been driven largely by the expanding scope and global reach of the industry, global regulatory environment and intelligence, scientific breakthrough and innovation, cutting-edge technologies including e-submissions, complexity of disease area targets for development and multiple stakeholder demand for rigorous and competitive product differentiation. These have heightened the need for highly-skilled regulatory professionals with area specialization and broad leadership capability.

In this changing and enhanced regulatory role, the regulatory team is expected to provide regulatory leadership and excellence in a changing environment. It requires the regulatory team to have at the core of its focus the end deliverable goal, which is expeditious patient access to high-quality, well-differentiated products.

This end goal drives the need for the regulatory team to:

- Deliver innovative, breakthrough regulatory strategies for product development and registration.
- Become more anticipatory of the company success imperatives.
- Be proactive and forward thinking, provide timely, comprehensive and robust global regulatory guidance.
- Understand the biopharmaceutical environment and regulatory actions on precedents and utilize such regulatory intelligence.
- Forge new standards to deliver more predictable outcomes.
- Increase focus on building and strengthening relationship with regulatory authorities to provide timely expert input into product development, manufacturing and registration.

From bench...

- IND/Clinical Trial Applications
- Regulatory strategy supporting company drug development and registration plans
- Leading interactions with regulatory authorities throughout development and registration phases
- Planning and preparation for regulatory meetings
- Coordination, review and electronic publishing of all regulatory review process through approval...

To bedside, and beyond...

- Management of compliance to post-marketing commitments and promotional/advertising regulations
- Management of the Life Cycle Optimization

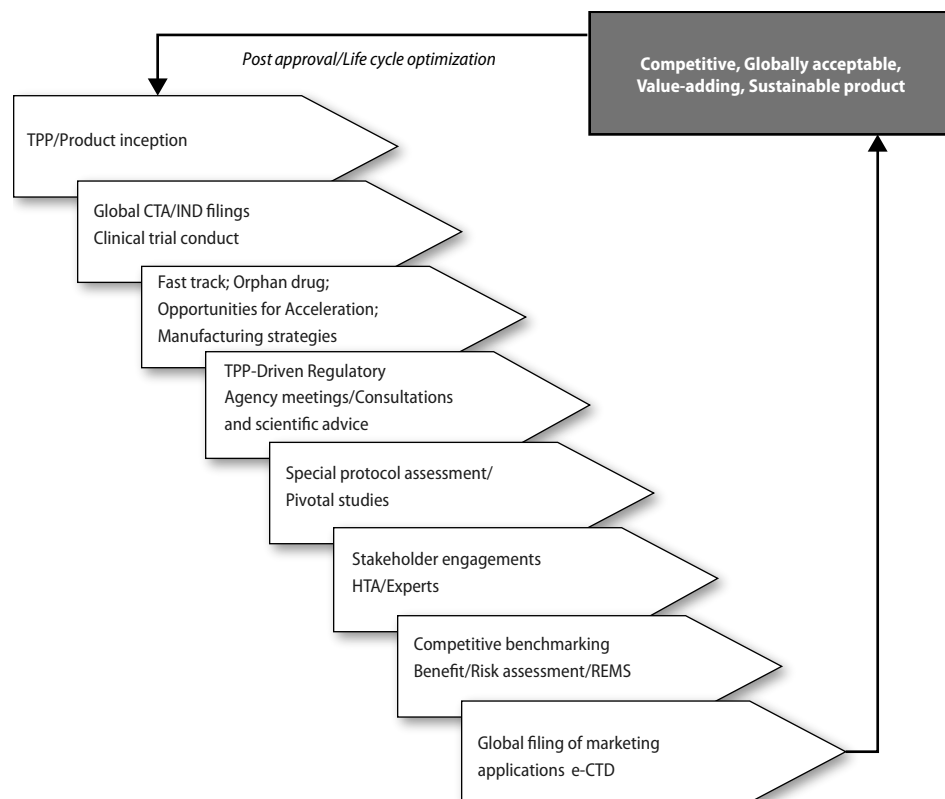
From bench to bedside, and beyond

The role of global regulatory affairs in industry spans from the inception of the product from development for human use, through registration, market viability and life cycle optimization. The corporate milestones mirror the regulatory key activities and events for product development. Regulatory teams develop and plan milestones and timelines to achieve strategic goals along the product development continuum. The regulatory teams need to have comprehensive knowledge of the global regulatory systems and strategically contribute such intelligence to product development and registration.

Regulatory teams are involved from the earliest development of a product's aspirational target profile through filing of clinical trials applications, successful conduct of studies, exploring

opportunities for acceleration of development such as orphan drug and fast track designations, engagement with the regulatory agencies to discuss development proposals through regulatory agency meetings, special protocol assessments, scientific advice, filing the marketing applications and regulatory reviews through product approval and life cycle optimization of the product.

Figure 2.1 Strategic elements of regulatory contribution



These become pivotal company milestones and metrics for assessing progress and quantifying and qualifying company success. The product life cycle optimization extends the life of the product, enhances value to patients and generates continued revenue from the product to the company. New formulations, dosages or regimens of the products are introduced, new and additional indications for product use are developed and combination strategies for synergies in treatment potential or convenience for patient use are addressed. Regulatory intelligence and strategy are useful and important in determining the regulatory pathway and prioritization for such optimization plans.

The global regulatory teams are uniquely positioned to actively participate in setting direction, guiding the progress and decision making at critical milestones for the product. They engage with regulatory authorities and internal stakeholders to enable product navigation from the laboratory bench to bedside. In addition, regulatory teams contribute to anticipating and managing global business risk, of which many are regulated activities.

As industry has turned its attention to global development for globally acceptable products, global regulatory affairs has become a crucial channel for communicating interdependencies of global regulatory agencies and requirements. A comprehensive and strategic approach to the complex interplay of key global regulatory systems and processes in developing and executing global regulatory strategies has become imperative to success.

In this era of extensive information flow across regulatory agencies with memoranda of understanding, regulatory agency decision-making on applications has become more interactive and transparent, appropriately so, as the application information is harmonized both in content and format via ICH Common Technical Document (CTD). Therefore, the regulatory teams must sharpen their global responsibility and input into the regulatory plans and strategies while

Corporate Product Development Milestones

- IND
- End of phase II
- Phase III start
- NDA/BLA filing
- Regulatory plan of action

Corporate decisions are made based on critical regulatory assessments.